



## Clinical trial results:

### A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study of Ustekinumab in Subjects with Active Systemic Lupus Erythematosus

#### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2017-001489-53       |
| Trial protocol           | ES LT DE BG HU PL PT |
| Global end of trial date | 05 November 2020     |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 21 May 2021  |
| First version publication date | 21 May 2021  |

#### Trial information

##### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | CNT01275SLE3001 |
|-----------------------|-----------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03517722 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Janssen Research and Development, LLC  |
| Sponsor organisation address | Welsh & McKean Roads, P.O. Box 776, Spring House, United States, PA 19477                    |
| Public contact               | Clinical Registry Group, Janssen Research and Development, LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry Group, Janssen Research and Development, LLC, ClinicalTrialsEU@its.jnj.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                       | 05 November 2020 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 05 November 2020 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of ustekinumab in subjects with active systemic lupus erythematosus (SLE) who had not adequately responded to one or more standard-of-care treatments.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices and applicable regulatory requirements. The safety assessments included vital signs, general and targeted physical examination, adverse events (AEs)/serious adverse events (SAEs), study agent administration reaction, concomitant medications, laboratory tests including pregnancy testing, chemistry, coagulation, hematology, and urinalysis, and immunogenicity.

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 03 May 2018 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | Yes         |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Argentina: 28          |
| Country: Number of subjects enrolled | Bulgaria: 27           |
| Country: Number of subjects enrolled | Canada: 2              |
| Country: Number of subjects enrolled | China: 8               |
| Country: Number of subjects enrolled | Colombia: 17           |
| Country: Number of subjects enrolled | Germany: 19            |
| Country: Number of subjects enrolled | Hungary: 14            |
| Country: Number of subjects enrolled | Japan: 46              |
| Country: Number of subjects enrolled | Lithuania: 21          |
| Country: Number of subjects enrolled | Poland: 38             |
| Country: Number of subjects enrolled | Portugal: 1            |
| Country: Number of subjects enrolled | Korea, Republic of: 5  |
| Country: Number of subjects enrolled | Russian Federation: 30 |
| Country: Number of subjects enrolled | Serbia: 42             |
| Country: Number of subjects enrolled | Spain: 10              |
| Country: Number of subjects enrolled | South Africa: 12       |
| Country: Number of subjects enrolled | Taiwan: 25             |

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Thailand: 12       |
| Country: Number of subjects enrolled | Ukraine: 30        |
| Country: Number of subjects enrolled | United States: 129 |
| Worldwide total number of subjects   | 516                |
| EEA total number of subjects         | 130                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                 | 4   |
| Adults (18-64 years)                      | 485 |
| From 65 to 84 years                       | 27  |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 1029 subjects were screened, out of which 516 subjects were randomized to the study. Out of 516, 208 subjects were randomized to placebo and 308 subjects were randomized to ustekinumab.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Through Week 52         |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Investigator, Subject   |

### Arms

|  |                                   |
|--|-----------------------------------|
| Are arms mutually exclusive?           | Yes                               |
| <b>Arm title</b>                       | Placebo - Ustekinumab             |
| Arm description: -                     |                                   |
| Arm type                               | Placebo                           |
| Investigational medicinal product name | Placebo                           |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Solution for infusion             |
| Routes of administration               | Intravenous use, Subcutaneous use |

Dosage and administration details:

Subjects received matching placebo to ustekinumab IV at Week 0, followed by matching placebo to ustekinumab SC at Week 8 and q8w thereafter through Week 48 during double-blind period. Eligible subjects who entered the extension period will cross-over to receive 90 mg ustekinumab SC q8w through Week 160.

|  |                                   |
|--|-----------------------------------|
| <b>Arm title</b>                       | Ustekinumab                       |
| Arm description: -                     |                                   |
| Arm type                               | Experimental                      |
| Investigational medicinal product name | Ustekinumab                       |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Solution for infusion             |
| Routes of administration               | Intravenous use, Subcutaneous use |

Dosage and administration details:

Subjects received ustekinumab approximately 6 milligram per kilogram (mg/kg) intravenously (IV) based on body weight-range at Week 0 followed by 90 mg ustekinumab subcutaneously (SC) at Week 8 and every 8 weeks (q8w) thereafter through Week 48 during double-blind period. Eligible subjects who will enter the extension period will continue to receive 90 mg ustekinumab SC q8w through Week 160.

| Number of subjects in period 1   | Placebo - Ustekinumab | Ustekinumab |
|----------------------------------|-----------------------|-------------|
| Started                          | 208                   | 308         |
| Completed                        | 105                   | 153         |
| Not completed                    | 103                   | 155         |
| Adverse event, serious fatal     | 1                     | 4           |
| Consent withdrawn by subject     | 11                    | 11          |
| Adverse event, non-fatal         | 2                     | 3           |
| Initiated prohibited medication  | -                     | 2           |
| Other                            | 4                     | 3           |
| Pregnancy                        | -                     | 1           |
| Study terminated by sponsor      | 76                    | 120         |
| Serious Adverse Event, non-fatal | 6                     | 8           |
| Lack of efficacy                 | 2                     | 3           |
| Protocol deviation               | 1                     | -           |

## Period 2

|                              |                         |
|------------------------------|-------------------------|
| Period 2 title               | After Week 52           |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Subject, Investigator   |

## Arms

|  |                                   |
|--|-----------------------------------|
| Are arms mutually exclusive?   | Yes                               |
| <b>Arm title</b>   | Placebo - Ustekinumab             |
| Arm description: -   |                                   |
| Arm type   | Placebo                           |
| Investigational medicinal product name   | Placebo                           |
| Investigational medicinal product code   |                                   |
| Other name   |                                   |
| Pharmaceutical forms   | Solution for infusion             |
| Routes of administration   | Intravenous use, Subcutaneous use |
| Dosage and administration details:   |                                   |
| Subjects received matching placebo to ustekinumab IV at Week 0, followed by matching placebo to ustekinumab SC at Week 8 and q8w thereafter through Week 48 during double-blind period. Eligible subjects who entered the extension period will cross-over to receive 90 mg ustekinumab SC q8w through Week 160. |                                   |
| <b>Arm title</b>   | Ustekinumab                       |
| Arm description: -   |                                   |
| Arm type   | Experimental                      |

|  |                                   |
|--|-----------------------------------|
| Investigational medicinal product name | Ustekinumab                       |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Solution for infusion             |
| Routes of administration               | Intravenous use, Subcutaneous use |

Dosage and administration details:

Subjects received ustekinumab approximately 6 milligram per kilogram (mg/kg) intravenously (IV) based on body weight-range at Week 0 followed by 90 mg ustekinumab subcutaneously (SC) at Week 8 and every 8 weeks (q8w) thereafter through Week 48 during double-blind period. Eligible subjects who will enter the extension period will continue to receive 90 mg ustekinumab SC q8w through Week 160.

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Placebo - Ustekinumab | Ustekinumab |
|---|-----------------------|-------------|
| Started   | 88                    | 137         |
| Completed   | 0                     | 0           |
| Not completed                                       | 88                    | 137         |
| Consent withdrawn by subject                        | 1                     | 1           |
| Study terminated by sponsor                         | 87                    | 134         |
| Serious Adverse Event, non-fatal                    | -                     | 1           |
| Lack of efficacy                                    | -                     | 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: These are the subjects who entered the extension phase at Week 52.

## Baseline characteristics

### Reporting groups

|                                |                       |
|--------------------------------|-----------------------|
| Reporting group title          | Placebo - Ustekinumab |
| Reporting group description: - |                       |
| Reporting group title          | Ustekinumab           |
| Reporting group description: - |                       |

| Reporting group values                      | Placebo -<br>Ustekinumab | Ustekinumab | Total |
|---|--------------------------|-------------|-------|
| Number of subjects                          | 208                      | 308         | 516   |
| Title for AgeCategorical<br>Units: subjects |                          |             |       |
| Children (2-11 years)                       | 0                        | 0           | 0     |
| Adolescents (12-17 years)                   | 3                        | 1           | 4     |
| Adults (18-64 years)                        | 191                      | 294         | 485   |
| From 65 to 84 years                         | 14                       | 13          | 27    |
| 85 years and over                           | 0                        | 0           | 0     |
| Title for AgeContinuous<br>Units: years     |                          |             |       |
| arithmetic mean                             | 44.5                     | 42.9        |       |
| standard deviation                          | ± 12.31                  | ± 11.38     | -     |
| Title for Gender<br>Units: subjects         |                          |             |       |
| Female                                      | 191                      | 291         | 482   |
| Male  | 17                       | 17          | 34    |

## End points

### End points reporting groups

|                                |                       |
|--------------------------------|-----------------------|
| Reporting group title          | Placebo - Ustekinumab |
| Reporting group description: - |                       |
| Reporting group title          | Ustekinumab           |
| Reporting group description: - |                       |
| Reporting group title          | Placebo - Ustekinumab |
| Reporting group description: - |                       |
| Reporting group title          | Ustekinumab           |
| Reporting group description: - |                       |

### Primary: Percentage of Subjects Achieving an Systemic Lupus Erythematosus Responder Index-4 (SRI-4) Composite Response at Week 52

|                        |   |
|------------------------|---|
| End point title        | Percentage of Subjects Achieving an Systemic Lupus Erythematosus Responder Index-4 (SRI-4) Composite Response at Week 52 <sup>[1]</sup> |
| End point description: |   |
| End point type         | Primary   |
| End point timeframe:   |   |
| Week 52                |   |

Notes:

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

Justification: No formal statistical hypothesis testing was planned for this study due to the descriptive nature of this study.

| End point values              | Placebo - Ustekinumab | Ustekinumab     |  |  |
|-------------------------------|-----------------------|-----------------|--|--|
| Subject group type            | Reporting group       | Reporting group |  |  |
| Number of subjects analysed   | 116                   | 173             |  |  |
| Units: percentage of subjects |                       |                 |  |  |
| number (not applicable)       | 65                    | 76              |  |  |

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Week 182

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Placebo (Prior to entering LTE) |
|-----------------------|---------------------------------|

Reporting group description:

Subjects only received placebo administration through Week 52 double blinded period. Data prior to the first administration of ustekinumab, or through the last follow-up if the subject did not receive any ustekinumab, were included.

|                       |   |
|-----------------------|---|
| Reporting group title | Placebo to Ustekinumab (After entering LTE) |
|-----------------------|---|

Reporting group description:

Subjects only received placebo administration through Week 52 double blinded period, and crossed over to ustekinumab in the extension period. Data from the first administration of ustekinumab through the last follow-up were included.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Ustekinumab (Through Week 176) |
|-----------------------|--------------------------------|

Reporting group description:

Subjects received ustekinumab administration through Week 52 double blinded period, and continued to receive ustekinumab in the extension period. Data from the first administration of ustekinumab through the last follow-up were included.

| Serious adverse events  | Placebo (Prior to entering LTE) | Placebo to Ustekinumab (After entering LTE) | Ustekinumab (Through Week 176) |
|---|---------------------------------|---|--------------------------------|
| Total subjects affected by serious adverse events                   |                                 |   |                                |
| subjects affected / exposed   | 28 / 208 (13.46%)               | 5 / 88 (5.68%)                              | 44 / 307 (14.33%)              |
| number of deaths (all causes)                                       | 1                               | 0   | 5                              |
| number of deaths resulting from adverse events                      |                                 |   |                                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                 |   |                                |
| Acoustic Neuroma  |                                 |   |                                |
| subjects affected / exposed   | 0 / 208 (0.00%)                 | 0 / 88 (0.00%)                              | 1 / 307 (0.33%)                |
| occurrences causally related to treatment / all                     | 0 / 0                           | 0 / 0                                       | 0 / 1                          |
| deaths causally related to treatment / all                          | 0 / 0                           | 0 / 0                                       | 0 / 0                          |
| Diffuse Large B-Cell Lymphoma                                       |                                 |   |                                |
| subjects affected / exposed   | 1 / 208 (0.48%)                 | 0 / 88 (0.00%)                              | 0 / 307 (0.00%)                |
| occurrences causally related to treatment / all                     | 1 / 1                           | 0 / 0                                       | 0 / 0                          |
| deaths causally related to treatment / all                          | 0 / 0                           | 0 / 0                                       | 0 / 0                          |
| Gastric Cancer  |                                 |   |                                |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| 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 disorders                              |                 |                |                 |
| Aortic Aneurysm                                 |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 1 / 88 (1.14%) | 0 / 307 (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           |
| Deep Vein Thrombosis                            |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 1 / 88 (1.14%) | 0 / 307 (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           |
| Hypotension                                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Hypovolaemic Shock                              |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Lupus Vasculitis                                |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pregnancy, puerperium and perinatal conditions  |                 |                |                 |
| Hyperemesis Gravidarum                          |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Reproductive system and breast disorders        |                 |                |                 |
| Benign Prostatic Hyperplasia                    |                 |                |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Ovarian Cyst                                    |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                |                 |
| Acute Respiratory Failure                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 2 / 307 (0.65%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Lupus Pleurisy                                  |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pleural Effusion                                |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pneumonitis                                     |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Pulmonary Hypertension                          |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Respiratory Failure                             |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |                |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Fall  |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Implantation Complication                       |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Infusion Related Reaction                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Patella Fracture                                |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Post Procedural Fever                           |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 1 / 88 (1.14%) | 0 / 307 (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           |
| Post Procedural Haemorrhage                     |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Splenic Rupture                                 |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0           |
| Ulna Fracture                                   |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Cardiac disorders                               |                 |                |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Acute Myocardial Infarction                     |                 |                |                 |
| subjects affected / exposed                     | 2 / 208 (0.96%) | 1 / 88 (1.14%) | 0 / 307 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Bradycardia                                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 1 / 88 (1.14%) | 0 / 307 (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           |
| Cardiac Failure                                 |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 2 / 307 (0.65%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Pericardial Effusion                            |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Nervous system disorders                        |                 |                |                 |
| Amnesia   |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Embololic Stroke                                |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Facial Paralysis                                |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Haemorrhagic Stroke                             |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Neuropsychiatric Lupus                          |                 |                |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 2 / 307 (0.65%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Seizure   |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Blood and lymphatic system disorders            |                 |                |                 |
| Thrombocytopenia                                |                 |                |                 |
| subjects affected / exposed                     | 2 / 208 (0.96%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Eye disorders                                   |                 |                |                 |
| Retinal Detachment                              |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Visual Impairment                               |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 1 / 88 (1.14%) | 0 / 307 (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           |
| Gastrointestinal disorders                      |                 |                |                 |
| Abdominal Hernia                                |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Abdominal Pain                                  |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Colitis   |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Gastritis                                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pancreatitis Acute                              |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Small Intestinal Obstruction                    |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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                         |                 |                |                 |
| Hepatorenal Syndrome                            |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                 |                |                 |
| Dermal Cyst                                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Hypersensitivity Vasculitis                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pemphigoid                                      |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Toxic Epidermal Necrolysis                      |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Renal and urinary disorders                     |                 |                |                 |
| Haematuria                                      |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Hydronephrosis                                  |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Lupus Nephritis                                 |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Nephritic Syndrome                              |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Nephrolithiasis                                 |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 2 / 307 (0.65%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Neurogenic Bladder                              |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Renal Colic                                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |                |                 |
| Intervertebral Disc Protrusion                  |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |



|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Osteonecrosis                                   |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Systemic Lupus Erythematosus                    |                 |                |                 |
| subjects affected / exposed                     | 4 / 208 (1.92%) | 0 / 88 (0.00%) | 2 / 307 (0.65%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                 |                |                 |
| Bronchitis                                      |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Covid-19  |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 4 / 307 (1.30%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Diverticulitis                                  |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Endocarditis Staphylococcal                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Gastroenteritis                                 |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 2 / 307 (0.65%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Herpes Zoster                                   |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (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           |
| Infected Bite                                   |                 |                |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Nosocomial Infection                            |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pneumonia                                       |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 4 / 307 (1.30%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 2 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pulmonary Tuberculosis                          |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Sepsis  |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Tonsillitis                                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Urinary Tract Infection                         |                 |                |                 |
| subjects affected / exposed                     | 2 / 208 (0.96%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Urosepsis                                       |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Viral Infection                                 |                 |                |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 0 / 307 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| <b>Vulval Cellulitis</b>                        |                 |                |                 |
| subjects affected / exposed                     | 0 / 208 (0.00%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| <b>Metabolism and nutrition disorders</b>       |                 |                |                 |
| <b>Electrolyte Imbalance</b>                    |                 |                |                 |
| subjects affected / exposed                     | 1 / 208 (0.48%) | 0 / 88 (0.00%) | 1 / 307 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 1           |
| 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>                            | Placebo (Prior to entering LTE) | Placebo to Ustekinumab (After entering LTE) | Ustekinumab (Through Week 176) |
|--|---------------------------------|---|--------------------------------|
| <b>Total subjects affected by non-serious adverse events</b> |                                 |   |                                |
| subjects affected / exposed                                  | 60 / 208 (28.85%)               | 3 / 88 (3.41%)                              | 79 / 307 (25.73%)              |
| <b>Nervous system disorders</b>                              |                                 |   |                                |
| <b>Headache</b>  |                                 |   |                                |
| subjects affected / exposed                                  | 14 / 208 (6.73%)                | 1 / 88 (1.14%)                              | 19 / 307 (6.19%)               |
| occurrences (all)  | 15                              | 1   | 42                             |
| <b>Infections and infestations</b>                           |                                 |   |                                |
| <b>Nasopharyngitis</b>                                       |                                 |   |                                |
| subjects affected / exposed                                  | 19 / 208 (9.13%)                | 2 / 88 (2.27%)                              | 24 / 307 (7.82%)               |
| occurrences (all)  | 23                              | 2   | 32                             |
| <b>Upper Respiratory Tract Infection</b>                     |                                 |   |                                |
| subjects affected / exposed                                  | 17 / 208 (8.17%)                | 0 / 88 (0.00%)                              | 25 / 307 (8.14%)               |
| occurrences (all)  | 21                              | 0   | 31                             |
| <b>Urinary Tract Infection</b>                               |                                 |   |                                |
| subjects affected / exposed                                  | 20 / 208 (9.62%)                | 0 / 88 (0.00%)                              | 26 / 307 (8.47%)               |
| occurrences (all)  | 25                              | 0   | 34                             |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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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.

|  |
|--|
| Study was early terminated for futility. |
|--|

Notes: