



Clinical trial results:

A Multi-center, Uncontrolled Extension Study Evaluating Efficacy and Safety of SAR153191 in Patients With Active Rheumatoid Arthritis (RA) Summary

| | |
|--------------------------|--|
| EudraCT number | 2010-019262-86 |
| Trial protocol | ES FI EE HU NL DE GR NO LT CZ IT AT PT SK GB BE SE |
| Global end of trial date | 31 December 2020 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 (current) |
| This version publication date | 06 January 2023 |
| First version publication date | 11 January 2022 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data setUpdated safety optional field |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | LTS11210 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01146652 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sanofi-aventis Recherche & Développement |
| Sponsor organisation address | 1 avenue Pierre Brossolette, Chilly Mazarin Cedex, France, 91380 |
| Public contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 08 February 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 December 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety of sarilumab in subjects with RA.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy:

Subjects who completed any of the initial studies EFC11072 (2009-016266-90), ACT11575 (2010-021020-94), EFC10832 (2011-003538-16), SFY13370 (2012-003536-23), EFC13752 (2013-002790-22) were enrolled in study LTS11210.

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 21 June 2010 |
| 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 | Australia: 26 |
| Country: Number of subjects enrolled | Belarus: 11 |
| Country: Number of subjects enrolled | Canada: 10 |
| Country: Number of subjects enrolled | Colombia: 61 |
| Country: Number of subjects enrolled | Sweden: 1 |
| Country: Number of subjects enrolled | Taiwan: 2 |
| Country: Number of subjects enrolled | Austria: 1 |
| Country: Number of subjects enrolled | Chile: 123 |
| Country: Number of subjects enrolled | Greece: 3 |
| Country: Number of subjects enrolled | Israel: 6 |
| Country: Number of subjects enrolled | Korea, Republic of: 36 |
| Country: Number of subjects enrolled | Mexico: 223 |
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | New Zealand: 18 |
| Country: Number of subjects enrolled | Poland: 224 |
| Country: Number of subjects enrolled | Thailand: 2 |

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | Italy: 3 |
| Country: Number of subjects enrolled | Peru: 43 |
| Country: Number of subjects enrolled | Portugal: 1 |
| Country: Number of subjects enrolled | Brazil: 65 |
| Country: Number of subjects enrolled | Czechia: 31 |
| Country: Number of subjects enrolled | Estonia: 36 |
| Country: Number of subjects enrolled | Malaysia: 3 |
| Country: Number of subjects enrolled | Philippines: 6 |
| Country: Number of subjects enrolled | Ukraine: 60 |
| Country: Number of subjects enrolled | South Africa: 85 |
| Country: Number of subjects enrolled | Argentina: 182 |
| Country: Number of subjects enrolled | Guatemala: 12 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Romania: 46 |
| Country: Number of subjects enrolled | Spain: 36 |
| Country: Number of subjects enrolled | Finland: 9 |
| Country: Number of subjects enrolled | Hungary: 70 |
| Country: Number of subjects enrolled | Russian Federation: 228 |
| Country: Number of subjects enrolled | Turkey: 1 |
| Country: Number of subjects enrolled | United States: 284 |
| Country: Number of subjects enrolled | Germany: 39 |
| Country: Number of subjects enrolled | Ecuador: 11 |
| Country: Number of subjects enrolled | Lithuania: 12 |
| Worldwide total number of subjects | 2023 |
| EEA total number of subjects | 514 |

Notes:

Subjects enrolled per age group

| | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 1732 |
| From 65 to 84 years | 290 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

2023 subjects who completed any of studies EFC11072, ACT11575, EFC10832, SFY13370, EFC13752 were eligible and enrolled in study LTS11210 between 21-Jun-2010 and 04-May-2015. From Week 24 of LTS11210, willing subjects were enrolled in a 12-week sub-study (part of main study only) to assess usability of pre-filled syringe with safety system (PFS-S).

Pre-assignment

Screening details:

Exposure to sarilumab: for 12 weeks (W) if they were initially randomised (R) in EFC11072 Part A or ACT11575; up to 52 W if initially R in EFC11072 Part B; up to 24 W if initially R in EFC10832; or for 24 W if initially R in SFY13370 or EFC13752. Subject's end-of-treatment visit in initial study corresponded to initial visit in study LTS11210.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) |

Arm description:

Subjects who completed any of initial studies: Part A or B of EFC11072, ACT11575, EFC10832 or SFY13370 were enrolled in LTS11210 and received sarilumab 150 milligrams (mg) subcutaneously (SC) once weekly (qw). Dose could be reduced to 150 mg every 2 weeks (q2w) due to neutropenia, thrombocytopenia or increase in liver enzymes (alanine aminotransferase [ALT]). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), subjects already receiving 150 mg qw were switched to sarilumab 200 mg q2w. Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks). Subjects who were already taking concomitant non-biologic DMARDs in initial study continued stable dose of one or combination of conventional synthetic DMARDs they were taking.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Sarilumab |
| Investigational medicinal product code | SAR153191 (REGN88) |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Sarilumab 150 mg, SC injection qw. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), 150 mg qw was switched to sarilumab 200 mg q2w.

| | |
|------------------|-----------------------|
| Arm title | Sarilumab monotherapy |
|------------------|-----------------------|

Arm description:

Subjects who completed study EFC13752 were enrolled in LTS11210 and received sarilumab 200 mg q2w. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks).

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

| | |
|--|------------------------|
| Investigational medicinal product name | Sarilumab |
| Investigational medicinal product code | SAR153191 (REGN88) |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Sarilumab 150 mg, SC injection qw. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), 150 mg qw was switched to sarilumab 200 mg q2w.

| Number of subjects in period 1 | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy |
|---------------------------------|--|-----------------------|
| | | |
| Started | 1912 | 111 |
| Treated | 1910 | 111 |
| Enrolled in the sub-study | 110 ^[1] | 14 ^[2] |
| Discontinued from the sub-study | 1 ^[3] | 2 ^[4] |
| Switched back to main study | 108 ^[5] | 13 ^[6] |
| Completed | 961 | 66 |
| Not completed | 951 | 45 |
| Adverse event, non-fatal | 506 | 15 |
| Poor compliance to protocol | 38 | 1 |
| Other unspecified reasons | 314 | 22 |
| Enrolled but not treated | 2 | - |
| Lack of efficacy | 91 | 7 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects who were eligible and entered sub-study from Week 24 of main study.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects who were eligible and entered sub-study from Week 24 of main study.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Sub-study discontinued subjects were included in the discontinuation count of the main study.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Sub-study discontinued subjects were included in the discontinuation count of the main study.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects who were willing to switch back to the main study regardless of if they completed the sub-study.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Subjects who were willing to switch back to the main study regardless of if they completed the sub-study.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) |
|-----------------------|--|

Reporting group description:

Subjects who completed any of initial studies: Part A or B of EFC11072, ACT11575, EFC10832 or SFY13370 were enrolled in LTS11210 and received sarilumab 150 milligrams (mg) subcutaneously (SC) once weekly (qw). Dose could be reduced to 150 mg every 2 weeks (q2w) due to neutropenia, thrombocytopenia or increase in liver enzymes (alanine aminotransferase [ALT]). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), subjects already receiving 150 mg qw were switched to sarilumab 200 mg q2w. Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks). Subjects who were already taking concomitant non-biologic DMARDs in initial study continued stable dose of one or combination of conventional synthetic DMARDs they were taking.

| | |
|-----------------------|-----------------------|
| Reporting group title | Sarilumab monotherapy |
|-----------------------|-----------------------|

Reporting group description:

Subjects who completed study EFC13752 were enrolled in LTS11210 and received sarilumab 200 mg q2w. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks).

| Reporting group values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | Total |
|------------------------------------|--|-----------------------|-------|
| Number of subjects | 1912 | 111 | 2023 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------|--------|------|
| Age continuous Units: years | | | |
| arithmetic mean | 52.1 | 52.9 | |
| standard deviation | ± 11.8 | ± 13.1 | - |
| Gender categorical Units: Subjects | | | |
| Female | 1550 | 88 | 1638 |
| Male | 362 | 23 | 385 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| Caucasian/White | 1639 | 108 | 1747 |
| Black | 48 | 1 | 49 |
| Asian/Oriental | 69 | 1 | 70 |
| Other | 156 | 1 | 157 |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) |
|-----------------------|--|

Reporting group description:

Subjects who completed any of initial studies: Part A or B of EFC11072, ACT11575, EFC10832 or SFY13370 were enrolled in LTS11210 and received sarilumab 150 milligrams (mg) subcutaneously (SC) once weekly (qw). Dose could be reduced to 150 mg every 2 weeks (q2w) due to neutropenia, thrombocytopenia or increase in liver enzymes (alanine aminotransferase [ALT]). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), subjects already receiving 150 mg qw were switched to sarilumab 200 mg q2w. Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks). Subjects who were already taking concomitant non-biologic DMARDs in initial study continued stable dose of one or combination of conventional synthetic DMARDs they were taking.

| | |
|-----------------------|-----------------------|
| Reporting group title | Sarilumab monotherapy |
|-----------------------|-----------------------|

Reporting group description:

Subjects who completed study EFC13752 were enrolled in LTS11210 and received sarilumab 200 mg q2w. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks).

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Sarilumab + DMARD: EFC11072 Part B |
|----------------------------|------------------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects who completed EFC11072 Part B were enrolled in LTS11210 and received sarilumab 150 mg SC qw. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), subjects already receiving 150 mg qw were switched to sarilumab 200 mg q2w. Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks). Subjects who were already taking concomitant non-biologic DMARDs in initial study continued stable dose of one or combination of conventional synthetic DMARDs they were taking.

| | |
|----------------------------|--|
| Subject analysis set title | Sarilumab + DMARD: EFC11072, ACT11575 and EFC10832 |
|----------------------------|--|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects who completed any of the initial studies: Part A or Part B of EFC11072, ACT11575, and EFC10832 were enrolled in LTS11210 and received sarilumab 150 mg SC qw. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), subjects already receiving 150 mg qw were switched to sarilumab 200 mg q2w. Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks). Subjects who were already taking concomitant non-biologic DMARDs in initial study continued stable dose of one or combination of conventional synthetic DMARDs they were taking.

| | |
|----------------------------|---|
| Subject analysis set title | Sarilumab + DMARD: EFC11072, and ACT11575 |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Subjects who completed any of the initial studies: Part A or Part B of EFC11072, and ACT11575 were enrolled in LTS11210 and received sarilumab 150 mg SC qw. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), subjects already receiving 150 mg qw were switched to sarilumab 200 mg q2w. Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks). Subjects who were already taking concomitant non-biologic DMARDs in initial study continued stable dose of one or combination of conventional synthetic DMARDs they were taking.

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | Sarilumab + DMARD: EFC10832 |
|----------------------------|-----------------------------|

| | |
|--|-----------------------------------|
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Subjects who completed study EFC10832 were enrolled in LTS11210 and received sarilumab 150 mg SC qw. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), subjects already receiving 150 mg qw were switched to sarilumab 200 mg q2w. Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks). Subjects who were already taking concomitant non-biologic DMARDs in initial study continued stable dose of one or combination of conventional synthetic DMARDs they were taking. | |
| Subject analysis set title | PFS-S Sarilumab 150 mg q2w |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| From Week 24 of main study, eligible subjects entered sub-study and received sarilumab 150 mg SC q2w for 12 weeks (i.e., from main study Week 24 to Week 36) using PFS-S. | |
| Subject analysis set title | PFS-S Sarilumab 200 mg q2w |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| From Week 24 of main study, eligible subjects entered sub-study and received sarilumab 200 mg SC q2w for 12 weeks (i.e., from main study Week 24 to Week 36) using PFS-S. | |
| Subject analysis set title | PFS-S Sarilumab 200 to 150 mg q2w |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| From Week 24 of main study, eligible subjects entered sub-study and received sarilumab 200 mg SC q2w for 12 weeks (i.e., from main study Week 24 to Week 36) using PF-S. The dose might be reduced to 150 mg q2w due to neutropenia, thrombocytopenia, or an increase in liver enzymes. | |

Primary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

| | |
|--|--|
| End point title | Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) ^[1] |
| End point description: | |
| An adverse event (AE) was any untoward medical occurrence in a clinical study subject administered a medicinal product and which did not necessarily have to have a causal relationship with the treatment. An SAE was any untoward medical occurrence at any dose that: resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a medically important event. TEAEs were AEs that developed or worsened or became serious during the TEAE period (defined as the time from the first dose of the investigational medicinal product (IMP) in study LTS11210 to the last dose of the IMP +60 days). Analysis was performed on safety population which included all enrolled subjects who had received at least one dose of the study treatment in LTS11210. | |
| End point type | Primary |
| End point timeframe: | |
| From first dose (i.e., Day 1 of study LTS11210) up to 60 days after last dose (maximum duration: up to 523 weeks) | |
| 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: As the end-point was descriptive in nature no statistical analysis was provided. | |

| End point values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|-----------------------------|--|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1910 | 111 | | |
| Units: subjects | | | | |

| | | | | |
|------------|------|----|--|--|
| Any TEAE | 1760 | 98 | | |
| Any TE SAE | 617 | 27 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Sub-study: Number of Subjects Reported Product Technical Complaints (PTC), Product Technical Failures (PTF) and/or Failed Drug Deliveries (FDD) With Pre-filled Syringe With Safety System

| | |
|-----------------|---|
| End point title | Sub-study: Number of Subjects Reported Product Technical Complaints (PTC), Product Technical Failures (PTF) and/or Failed Drug Deliveries (FDD) With Pre-filled Syringe With Safety System ^[2] |
|-----------------|---|

End point description:

A PTF was defined as any product technical complaint (PTC) related to the use of the PFS-S that had a validated technical cause. FDD was defined as subject's failure to administer the full dose at a given attempt. A PTC was defined as any subject- or healthcare provider-reported complaint regarding the use of the PFS-S syringe and collected via the completion of the injection diary. The injection diary comprised specific questions: 1. Were you able to remove the cap? 2. Was the needle safety system activated?, 3. Did the safety system entirely cover the needle, and 4. Was the person who performed the injection the person who was trained by the site staff?, where each question was given the option yes/no. Subjects who answered "no" for any of the questions of PTC, had PTF and/or FDD were reported in this endpoint. Analysis was performed on all subjects who were enrolled in the sub-study.

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

End point timeframe:

From Week 24 to 36

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: As the end-point was descriptive in nature no statistical analysis was provided.

| End point values | PFS-S Sarilumab 150 mg q2w | PFS-S Sarilumab 200 mg q2w | PFS-S Sarilumab 200 to 150 mg q2w | |
|-----------------------------|----------------------------------|----------------------------------|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 25 | 98 | 1 | |
| Units: subjects | | | | |
| PFS-S-associated PTF | 0 | 0 | 0 | |
| PFS-S-associated FDD | 0 | 5 | 0 | |
| PFS-S-associated PTC | 0 | 5 | 0 | |

Statistical analyses

No statistical analyses for this end point

Primary: Sub-study: Number of Product Technical Complaints - Product Technical Failures With Pre-filled Syringe With Safety System

| | |
|-----------------|--|
| End point title | Sub-study: Number of Product Technical Complaints - Product Technical Failures With Pre-filled Syringe With Safety System ^[3] |
|-----------------|--|

End point description:

A PTF was defined as any PTC (defined as any subject- or healthcare provider-reported complaint regarding the use of the PFS-S syringe and collected via the completion of the injection diary) related to the use of the PFS-S that had a validated technical cause. Number of PTF in the subjects enrolled in sub-study were reported in this endpoint. Analysis was performed on all subjects who were enrolled in the sub-study.

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

End point timeframe:

From Week 24 to 36

Notes:

[3] - 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: As the end-point was descriptive in nature no statistical analysis was provided.

| End point values | PFS-S Sarilumab 150 mg q2w | PFS-S Sarilumab 200 mg q2w | PFS-S Sarilumab 200 to 150 mg q2w | |
|-----------------------------|----------------------------------|----------------------------------|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 25 | 98 | 1 | |
| Units: PTF | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Primary: Sub-study: Number of Failed Drug Deliveries Associated With Pre-filled Syringe With Safety System

| | |
|-----------------|--|
| End point title | Sub-study: Number of Failed Drug Deliveries Associated With Pre-filled Syringe With Safety System ^[4] |
|-----------------|--|

End point description:

FDD was defined as subject's failure to administer the full dose at a given attempt. Number of FDD in the subjects enrolled in sub-study were reported in this endpoint. Analysis was performed on all subjects who were enrolled in the sub-study.

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

End point timeframe:

From Week 24 to 36

Notes:

[4] - 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: As the end-point was descriptive in nature no statistical analysis was provided.

| End point values | PFS-S Sarilumab 150 mg q2w | PFS-S Sarilumab 200 mg q2w | PFS-S Sarilumab 200 to 150 mg q2w | |
|-----------------------------|----------------------------------|----------------------------------|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 25 | 98 | 1 | |
| Units: FDD | 0 | 5 | 0 | |

Statistical analyses

Primary: Sub-study: Number of Product Technical Complaints With Pre-filled Syringe With Safety System

| | |
|-----------------|---|
| End point title | Sub-study: Number of Product Technical Complaints With Pre-filled Syringe With Safety System ^[5] |
|-----------------|---|

End point description:

A PTC was defined as any subject- or healthcare provider-reported complaint regarding the use of the PFS-S syringe and collected via the completion of the injection diary. The injection diary comprised specific questions: 1. Were you able to remove the cap? 2. Was the needle safety system activated?, 3. Did the safety system entirely cover the needle, and 4. Was the person who performed the injection the person who was trained by the site staff?, where each question was given the option yes/no. Number of PTC (based on subject's answer to "no" for any of the questions of PTC) in the subjects enrolled in sub-study were reported in this endpoint. Analysis was performed on all subjects who were enrolled in the sub-study.

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

End point timeframe:

From Week 24 to 36

Notes:

[5] - 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: As the end-point was descriptive in nature no statistical analysis was provided.

| End point values | PFS-S Sarilumab 150 mg q2w | PFS-S Sarilumab 200 mg q2w | PFS-S Sarilumab 200 to 150 mg q2w | |
|-----------------------------|----------------------------------|----------------------------------|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 25 | 98 | 1 | |
| Units: PTC | 0 | 5 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving American College of Rheumatology 20 (ACR20) Response

| | |
|-----------------|---|
| End point title | Percentage of Subjects Achieving American College of Rheumatology 20 (ACR20) Response |
|-----------------|---|

End point description:

ACR20 response: greater than or equal to (\geq) 20% improvement in both tender joint count and swollen joint count and \geq 20% improvement in at least 3 of 5 remaining ACR core measures assessments: C-reactive protein [CRP] level (mg/litre [mg/L]); subject's assessment of pain (measured on 0 [no pain] to 100 mm [worst pain] visual analog scale [VAS]); subject's global assessment of disease activity (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS); physician's global assessment of disease activity (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS); subject's assessment of physical function (measured by health assessment questionnaire disability index, with scoring range of 0 [better physical function] to 3 [worst physical function]). Higher score = worse outcomes. Safety population: subjects who had at least 1 dose of study treatment in LTS11210. Here, number of subjects analysed=subjects evaluable and n=subjects with data.

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

End point timeframe:

At Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + Disease Modifying Anti- Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|----------------------------------|--|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1898 | 111 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Week 0 (1898, 111) | 69.4 (67.3 to 71.5) | 82.0 (73.6 to 88.6) | | |
| Week 4 (n=1885, 106) | 77.8 (75.8 to 79.6) | 85.8 (77.7 to 91.9) | | |
| Week 8 (n=1852, 106) | 80.2 (78.3 to 82.0) | 92.5 (85.7 to 96.7) | | |
| Week 12 (n=1829, 109) | 80.3 (78.4 to 82.1) | 91.7 (84.9 to 96.2) | | |
| Week 24 (n=1787, 109) | 82.9 (81.1 to 84.6) | 88.1 (80.5 to 93.5) | | |
| Week 36 (n= 1730, 109) | 82.8 (80.9 to 84.5) | 91.7 (84.9 to 96.2) | | |
| Week 48 (n=1670, 107) | 82.9 (81.0 to 84.7) | 85.0 (76.9 to 91.2) | | |
| Week 60 (n=1618, 103) | 84.6 (82.8 to 86.3) | 93.2 (86.5 to 97.2) | | |
| Week 72 (n=1586, 101) | 84.4 (82.5 to 86.1) | 94.1 (87.5 to 97.8) | | |
| Week 84 (n=1550, 95) | 84.5 (82.6 to 86.2) | 94.7 (88.1 to 98.3) | | |
| Week 96 (n=1510, 92) | 85.2 (83.3 to 87.0) | 91.3 (83.6 to 96.2) | | |
| Week 120 (n=1456, 88) | 84.9 (82.9 to 86.7) | 90.9 (82.9 to 96.0) | | |
| Week 144 (n=1389, 83) | 86.4 (84.5 to 88.2) | 94.0 (86.5 to 98.0) | | |
| Week 168 (n=1322,81) | 86.0 (84.0 to 87.8) | 90.1 (81.5 to 95.6) | | |
| Week 192 (n=1263, 75) | 85.7 (83.7 to 87.6) | 89.3 (80.1 to 95.3) | | |
| Week 216 (n=1189, 74) | 87.1 (85.1 to 89.0) | 89.2 (79.8 to 95.2) | | |
| Week 240 (n=1125, 74) | 86.4 (84.3 to 88.4) | 91.9 (83.2 to 97.0) | | |
| Week 264 (n=1049, 61) | 88.5 (86.4 to 90.3) | 90.2 (79.8 to 96.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving American College of Rheumatology 50 (ACR50) Response

| | |
|---|---|
| End point title | Percentage of Subjects Achieving American College of Rheumatology 50 (ACR50) Response |
| End point description: | |
| ACR50 response: $\geq 50\%$ improvement in both TJC and SJC, and $\geq 50\%$ improvement in at least 3 of the 5 remaining ACR core measures assessments: CRP level (in mg/L); subject's assessment of pain (measured on 0 [no pain] to 100 mm [worst pain] VAS); subject's global assessment of disease activity (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS); physician's global assessment of disease activity (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS); subject's assessment of physical function (measured by HAQ-DI, with scoring range of 0 [better physical function] to 3 [worst physical function]). Higher score indicated worse outcomes. Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and 'n' = subjects with available data for each specified category. | |
| End point type | Secondary |
| End point timeframe: | |
| At Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 | |

| End point values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|----------------------------------|--|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1897 | 111 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Week 0 (n=1897, 111) | 43.4 (41.2 to 45.7) | 58.6 (48.8 to 67.8) | | |
| Week 4 (n=1884, 108) | 51.3 (49.0 to 53.6) | 59.3 (49.4 to 68.6) | | |
| Week 8 (n=1850, 105) | 55.1 (52.8 to 57.4) | 59.0 (49.0 to 68.5) | | |
| Week 12 (n=1830, 108) | 58.1 (55.8 to 60.4) | 66.7 (56.9 to 75.4) | | |
| Week 24 (n=1782, 109) | 60.5 (58.2 to 62.8) | 64.2 (54.5 to 73.2) | | |
| Week 36 (n=1729, 109) | 62.1 (59.8 to 64.4) | 64.2 (54.5 to 73.2) | | |
| Week 48 (n=1669, 107) | 62.4 (60.0 to 64.7) | 69.2 (59.5 to 77.7) | | |
| Week 60 (n=1620, 103) | 63.2 (60.8 to 65.6) | 68.9 (59.1 to 77.7) | | |
| Week 72 (n=1585, 101) | 64.8 (62.4 to 67.1) | 71.3 (61.4 to 79.9) | | |
| Week 84 (n=1546, 94) | 63.6 (61.2 to 66.1) | 73.4 (63.3 to 82.0) | | |
| Week 96 (n=1511, 92) | 65.3 (62.8 to 67.7) | 71.7 (61.4 to 80.6) | | |
| Week 120 (n=1455, 87) | 65.6 (63.1 to 68.0) | 73.6 (63.0 to 82.4) | | |
| Week 144 (n=1385, 84) | 65.7 (63.1 to 68.2) | 70.2 (59.3 to 79.7) | | |
| Week 168 (n=1320, 80) | 66.2 (63.6 to 68.8) | 70.0 (58.7 to 79.7) | | |
| Week 192 (n=1257, 75) | 68.4 (65.8 to 71.0) | 70.7 (59.0 to 80.6) | | |

| | | | | |
|-----------------------|---------------------|---------------------|--|--|
| Week 216 (n=1189, 74) | 69.0 (66.3 to 71.7) | 75.7 (64.3 to 84.9) | | |
| Week 240 (n=1125, 74) | 68.3 (65.5 to 71.0) | 79.7 (68.8 to 88.2) | | |
| Week 264 (n=1040, 60) | 69.6 (66.7 to 72.4) | 71.7 (58.6 to 82.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving American College of Rheumatology 70 (ACR70) Response

| | |
|-----------------|---|
| End point title | Percentage of Subjects Achieving American College of Rheumatology 70 (ACR70) Response |
|-----------------|---|

End point description:

ACR70 response: $\geq 70\%$ improvement in both TJC and SJC, and $\geq 70\%$ improvement in at least 3 of the 5 remaining ACR core measures assessments: CRP level (in mg/L); subject's assessment of pain (measured on 0 [no pain] to 100 mm [worst pain] VAS); subject's global assessment of disease activity (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS); physician's global assessment of disease activity (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS); subject's assessment of physical function (measured by HAQ-DI, with scoring range of 0 [better physical function] to 3 [worst physical function]). Higher score indicated worse outcomes. Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and 'n' = subject with available data for each specified category.

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

End point timeframe:

At Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|----------------------------------|--|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1901 | 111 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Week 0 (n=1901, 111) | 22.9 (21.0 to 24.8) | 32.4 (23.9 to 42.0) | | |
| Week 4 (n=1879, 108) | 27.8 (25.8 to 29.9) | 31.5 (22.9 to 41.1) | | |
| Week 8 (n=1854, 105) | 32.1 (30.0 to 34.3) | 36.2 (27.0 to 46.1) | | |
| Week 12 (n=1829, 107) | 34.1 (31.9 to 36.3) | 43.0 (33.5 to 52.9) | | |
| Week 24 (n=1781, 107) | 38.7 (36.4 to 41.0) | 37.4 (28.2 to 47.3) | | |
| Week 36 (n=1726, 109) | 40.2 (37.9 to 42.6) | 40.4 (31.1 to 50.2) | | |
| Week 48 (n=1666, 105) | 40.6 (38.3 to 43.0) | 43.8 (34.1 to 53.8) | | |

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|-----------------------|---------------------|---------------------|--|--|
| Week 60 (n=1618, 103) | 41.6 (39.2 to 44.0) | 45.6 (35.8 to 55.7) | | |
| Week 72 (n=1585, 100) | 42.1 (39.6 to 44.6) | 49.0 (38.9 to 59.2) | | |
| Week 84 (n=1541, 94) | 41.8 (39.3 to 44.3) | 52.1 (41.6 to 62.5) | | |
| Week 96 (n=1510, 92) | 43.4 (40.9 to 45.9) | 55.4 (44.7 to 65.8) | | |
| Week 120 (n=1449, 88) | 42.9 (40.3 to 45.5) | 56.8 (45.8 to 67.3) | | |
| Week 144 (n=1386, 84) | 44.7 (42.0 to 47.3) | 50.0 (38.9 to 61.1) | | |
| Week 168 (n=1317, 80) | 45.6 (42.9 to 48.4) | 51.3 (39.8 to 62.6) | | |
| Week 192 (n=1262, 76) | 47.9 (45.1 to 50.7) | 53.9 (42.1 to 65.5) | | |
| Week 216 (n=1186, 71) | 46.8 (43.9 to 49.7) | 62.0 (49.7 to 73.2) | | |
| Week 240 (n=1123, 74) | 47.9 (44.9 to 50.9) | 60.8 (48.8 to 72.0) | | |
| Week 264 (n=1030, 60) | 48.8 (45.7 to 51.9) | 58.3 (44.9 to 70.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Disease Activity Score for 28 Joints (DAS28) Remission

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|-----------------|--|
| End point title | Percentage of Subjects With Disease Activity Score for 28 Joints (DAS28) Remission |
|-----------------|--|

End point description:

Disease activity score based on 28 joints and C-reactive protein (DAS28-CRP) was a composite score which included 4 components: TJC with 28 joints assessed; SJC with 28 joints assessed; high-sensitivity CRP (in mg/L) and general health assessment by the subject using subject global assessment (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS). DAS28-CRP total score ranges from 0 to 10, where higher scores indicated greater disease activity. Percentage of subjects with DAS28 remission were reported. Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and n' = subject with available data for each specified category and "99999" was used as space filler which indicates that data was not planned to be collected and analysed for the specified time-points in the respective groups.

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

End point timeframe:

At Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| | | | | |
|-----------------------------|--|-----------------------|--|--|
| End point values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1873 | 110 | | |

| Units: percentage of subjects | | | | |
|----------------------------------|---------------------|------------------------|--|--|
| number (confidence interval 95%) | | | | |
| Week 0 (n=1873, 110) | 30.4 (28.3 to 32.5) | 46.4 (36.8 to 56.1) | | |
| Week 4 (n=1867, 106) | 39.2 (36.9 to 41.4) | 51.9 (42.0 to 61.7) | | |
| Week 8 (n=1804, 105) | 44.6 (42.3 to 46.9) | 49.5 (39.6 to 59.5) | | |
| Week 12 (n=1819, 109) | 47.9 (45.6 to 50.3) | 55.0 (45.2 to 64.6) | | |
| Week 24 (n=1778, 109) | 50.6 (48.2 to 52.9) | 59.6 (49.8 to 68.9) | | |
| Week 36 (n=1721, 109) | 51.7 (49.3 to 54.1) | 59.6 (49.8 to 68.9) | | |
| Week 48 (n=1661, 107) | 53.7 (51.3 to 56.1) | 56.1 (46.1 to 65.7) | | |
| Week 60 (n=1608, 102) | 56.5 (54.1 to 59.0) | 61.8 (51.6 to 71.2) | | |
| Week 72 (n=1580, 101) | 55.8 (53.3 to 58.3) | 68.3 (58.3 to 77.2) | | |
| Week 84 (n=1537, 95) | 55.8 (53.2 to 58.3) | 70.5 (60.3 to 79.4) | | |
| Week 96 (n=1506, 92) | 57.0 (54.5 to 59.6) | 71.7 (61.4 to 80.6) | | |
| Week 120 (n=1444, 88) | 59.2 (56.6 to 61.8) | 73.9 (63.4 to 82.7) | | |
| Week 144 (n=1381, 83) | 59.3 (56.7 to 61.9) | 72.3 (61.4 to 81.6) | | |
| Week 168 (n=1309, 81) | 59.7 (56.9 to 62.3) | 70.4 (59.2 to 80.0) | | |
| Week 192 (n=1250, 76) | 62.1 (59.3 to 64.8) | 67.1 (55.4 to 77.5) | | |
| Week 216 (n=1175, 73) | 63.6 (60.7 to 66.3) | 71.2 (59.4 to 81.2) | | |
| Week 240 (n=1118, 73) | 61.6 (58.7 to 64.5) | 82.2 (71.5 to 90.2) | | |
| Week 264 (n=1036, 62) | 64.4 (61.4 to 67.3) | 75.8 (63.3 to 85.8) | | |
| Week 288 (n=715, 26) | 68.7 (65.1 to 72.1) | 73.1 (52.2 to 88.4) | | |
| Week 312 (n=655, 7) | 69.0 (65.3 to 72.5) | 85.7 (42.1 to 99.6) | | |
| Week 336 (n=540, 0) | 72.2 (68.2 to 76.0) | 99999 (99999 to 99999) | | |
| Week 360 (n=424, 0) | 71.7 (67.2 to 75.9) | 99999 (99999 to 99999) | | |
| Week 384 (n=334, 0) | 71.6 (66.4 to 76.3) | 99999 (99999 to 99999) | | |
| Week 408 (n=199, 0) | 69.8 (63.0 to 76.1) | 99999 (99999 to 99999) | | |
| Week 432 (n=106, 0) | 76.4 (67.2 to 84.1) | 99999 (99999 to 99999) | | |
| Week 456 (n=55, 0) | 72.7 (59.0 to 83.9) | 99999 (99999 to 99999) | | |
| Week 480 (n=39, 0) | 76.9 (60.7 to 88.9) | 99999 (99999 to 99999) | | |
| Week 504 (n=26, 0) | 73.1 (52.2 to 88.4) | 99999 (99999 to 99999) | | |
| Week 516 (n=2, 0) | 50.0 (1.3 to 98.7) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects achieving Good Response, Moderate Response or Non-response Using the European League Against Rheumatism (EULAR) Response Criteria

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|-----------------|--|
| End point title | Percentage of Subjects achieving Good Response, Moderate Response or Non-response Using the European League Against Rheumatism (EULAR) Response Criteria |
|-----------------|--|

End point description:

DAS28-based EULAR response criteria measured individual response as none, good or moderate, depending on extent of change from baseline and level of disease activity reached. EULAR response criteria were defined as: Good response=change from baseline of >1.2 and present DAS28-CRP score ≤3.2. Moderate response=change from baseline of >0.6 to ≤1.2 and present DAS28-CRP score ≤5.1, or, change from baseline of >1.2 and present DAS28-CRP score >3.2. Non-response=change from baseline of ≤0.6 or change from baseline of >0.6 to ≤1.2 and present DAS28-CRP score >5.1. Scores of good and moderate=therapeutic response. DAS28-CRP: composite score which had 4 components: TJC with 28 joints assessed; SJC with 28 joints assessed; high-sensitivity CRP (in mg/L) and general health assessment by subject using subject global assessment (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS. Safety population. number of subjects=subjects evaluable and n=subjects with data.

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

End point timeframe:

At Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| End point values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|---|--|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1872 | 110 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 0: Good response (n=1872,110) | 44.7 | 60.9 | | |
| Week 0: Moderate response (n=1872, 110) | 40.3 | 30.9 | | |
| Week 0: None response (n=1872, 110) | 15.0 | 8.2 | | |
| Week 4: Good response (n=1866,106) | 57.2 | 69.8 | | |
| Week 4: Moderate response (n=1866,106) | 36.2 | 26.4 | | |
| Week 4:None response (n=1866,106) | 6.6 | 3.8 | | |
| Week 8: Good response (n=1803, 105) | 62.3 | 68.6 | | |
| Week 8: Moderate response (n=1803, 105) | 31.7 | 27.6 | | |
| Week 8: None response (n=1803, 105) | 6.0 | 3.8 | | |

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|--|------|------|--|--|
| Week 12: Good response (n=1818, 109) | 64.1 | 74.3 | | |
| Week 12: Moderate response (n=1818, 109) | 30.6 | 22.9 | | |
| Week 12: None response (n=1818, 109) | 5.2 | 2.8 | | |
| Week 24: Good response (n=1777, 109) | 66.6 | 73.4 | | |
| Week 24: Moderate response (n=1777, 109) | 28.9 | 24.8 | | |
| Week 24: None response (n=1777, 109) | 4.5 | 1.8 | | |
| Week 36: Good response (n=1720, 109) | 67.9 | 71.6 | | |
| Week 36: Moderate response (n=1720, 109) | 27.0 | 24.8 | | |
| Week 36: None response (n=1720, 109) | 5.1 | 3.7 | | |
| Week 48: Good response (n=1660, 107) | 68.1 | 72.0 | | |
| Week 48: Moderate response (n=1660, 107) | 27.4 | 24.3 | | |
| Week 48: None response (n=1660, 107) | 4.5 | 3.7 | | |
| Week 60: Good response (n=1607, 102) | 71.1 | 68.6 | | |
| Week 60: Moderate response (n=1607, 102) | 24.6 | 29.4 | | |
| Week 60: None response (n=1607, 102) | 4.2 | 2.0 | | |
| Week 72: Good response (n=1579, 101) | 70.0 | 81.2 | | |
| Week 72: Moderate response (n=1579, 101) | 26.0 | 16.8 | | |
| Week 72: None response (n=1579, 101) | 4.0 | 2.0 | | |
| Week 84: Good response (n=1536, 95) | 71.3 | 84.2 | | |
| Week 84: Moderate response (n=1536, 95) | 24.2 | 14.7 | | |
| Week 84: None response (n=1536, 95) | 4.6 | 1.1 | | |
| Week 96: Good response (n=1505, 92) | 72.6 | 76.1 | | |
| Week 96: Moderate response (n=1505, 92) | 23.3 | 21.7 | | |
| Week 96: None response (n=1505, 92) | 4.1 | 2.2 | | |
| Week 120: Good response (n=1443, 88) | 73.5 | 80.7 | | |
| Week 120: Moderate response (n=1443, 88) | 22.3 | 17.0 | | |
| Week 120: None response (n=1443, 88) | 4.2 | 2.3 | | |
| Week 144: Good response (n=1381, 83) | 73.3 | 86.7 | | |
| Week 144: Moderate response (n=1381, 83) | 22.8 | 13.3 | | |
| Week 144: None response (n=1381, 83) | 3.9 | 0 | | |
| Week 168: Good response (n=1309, 81) | 74.5 | 84.0 | | |
| Week 168: Moderate response (n=1309, 81) | 20.6 | 16.0 | | |
| Week 168: None response (n=1309, 81) | 4.9 | 0 | | |
| Week 192: Good response (n=1250, 76) | 75.6 | 81.6 | | |
| Week 192: Moderate response (n=1250, 76) | 20.6 | 13.2 | | |
| Week 192: None response (n=1250, 76) | 3.8 | 5.3 | | |

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|--|------|-------|--|--|
| Week 216: Good response (n=1175, 73) | 75.9 | 80.8 | | |
| Week 216: Moderate response (n=1175, 73) | 20.5 | 17.8 | | |
| Week 216: None response (n=1175, 73) | 3.6 | 1.4 | | |
| Week 240: Good response (n=1118, 73) | 78.6 | 89.0 | | |
| Week 240: Moderate response (n=1118, 73) | 17.5 | 9.6 | | |
| Week 240: None response (n=1118, 73) | 3.8 | 1.4 | | |
| Week 264: Good response (n=1036, 62) | 76.7 | 83.9 | | |
| Week 264: Moderate response (n=1036, 62) | 20.2 | 16.1 | | |
| Week 264: None response (n=1036, 62) | 3.1 | 0 | | |
| Week 288: Good response (n=715, 26) | 82.4 | 80.8 | | |
| Week 288: Moderate response (n=715, 26) | 15.2 | 19.2 | | |
| Week 288: None response (n=715, 26) | 2.4 | 0 | | |
| Week 312: Good response (n=655, 7) | 81.5 | 100 | | |
| Week 312: Moderate response (n=655, 7) | 16.3 | 0 | | |
| Week 312: None response (n=655, 7) | 2.1 | 0 | | |
| Week 336: Good response (n=540, 0) | 83.0 | 99999 | | |
| Week 336: Moderate response (n=540, 0) | 14.6 | 99999 | | |
| Week 336: None response (n=540, 0) | 2.4 | 99999 | | |
| Week 360: Good response (n=424, 0) | 83.3 | 99999 | | |
| Week 360: Moderate response (n=424, 0) | 15.1 | 99999 | | |
| Week 360: None response (n=424, 0) | 1.7 | 99999 | | |
| Week 384: Good response (n=334, 0) | 86.2 | 99999 | | |
| Week 384: Moderate response (n=334, 0) | 12.9 | 99999 | | |
| Week 384: None response (n=334, 0) | 0.9 | 99999 | | |
| Week 408: Good response (n=199, 0) | 81.9 | 99999 | | |
| Week 408: Moderate response (n=199, 0) | 16.1 | 99999 | | |
| Week 408: None response (n=199, 0) | 2.0 | 99999 | | |
| Week 432: Good response (n=106, 0) | 85.8 | 99999 | | |
| Week 432: Moderate response (n=106, 0) | 14.2 | 99999 | | |
| Week 432: None response (n=106, 0) | 0 | 99999 | | |
| Week 456: Good response (n=55, 0) | 87.3 | 99999 | | |
| Week 456: Moderate response (n=55, 0) | 12.7 | 99999 | | |
| Week 456: None response (n=55, 0) | 0 | 99999 | | |
| Week 480: Good response (n=39, 0) | 79.5 | 99999 | | |
| Week 480: Moderate response (n=39, 0) | 17.9 | 99999 | | |
| Week 480: None response (n=39, 0) | 2.6 | 99999 | | |
| Week 504: Good response (n=26, 0) | 92.3 | 99999 | | |
| Week 504: Moderate response (n=26, 0) | 7.7 | 99999 | | |
| Week 504: None response (n=26, 0) | 0 | 99999 | | |
| Week 516: Good response (n=2, 0) | 100 | 99999 | | |
| Week 516: Moderate response (n=2, 0) | 0 | 99999 | | |

| | | | | |
|----------------------------------|---|-------|--|--|
| Week 516: None response (n=2, 0) | 0 | 99999 | | |
|----------------------------------|---|-------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in DAS28-CRP Score at Weeks 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| | |
|-----------------|---|
| End point title | Change From Baseline in DAS28-CRP Score at Weeks 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210 |
|-----------------|---|

End point description:

DAS28-CRP is a composite score which included 4 components: TJC with 28 joints assessed; SJC with 28 joints assessed; high-sensitivity CRP (in mg/L) and general health assessment by the subject using subject global assessment (measured on 0 [no arthritis activity] to 100 mm [maximal arthritis activity] VAS). DAS28-CRP total score ranges from 0 to 10, where higher scores indicated greater disease activity. Here, Baseline refers to the Baseline of initial studies (EFC11072, ACT11575, EFC10832, SFY13370 and EFC13752). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and 'n' = subjects with available data for each specified category and "99999" was used as space filler which indicates that data was not planned to be collected and analysed for the specified time-points in the respective groups.

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

End point timeframe:

Baseline, Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| End point values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|--------------------------------------|--|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1872 | 110 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1872, 110) | -2.50 (± 1.52) | -2.99 (± 1.42) | | |
| Week 4 (n=1866, 106) | -2.98 (± 1.38) | -3.18 (± 1.31) | | |
| Week 8 (n=1803, 105) | -3.12 (± 1.41) | -3.21 (± 1.26) | | |
| Week 12 (n=1818, 109) | -3.19 (± 1.41) | -3.28 (± 1.29) | | |
| Week 24 (n=1777, 109) | -3.28 (± 1.41) | -3.43 (± 1.21) | | |
| Week 36 (n=1720, 109) | -3.31 (± 1.43) | -3.35 (± 1.23) | | |
| Week 48 (n=1660, 107) | -3.35 (± 1.42) | -3.36 (± 1.35) | | |
| Week 60 (n=1607, 102) | -3.41 (± 1.41) | -3.50 (± 1.28) | | |
| Week 72 (n=1579, 101) | -3.41 (± 1.42) | -3.61 (± 1.24) | | |
| Week 84 (n=1536, 95) | -3.40 (± 1.45) | -3.70 (± 1.19) | | |
| Week 96 (n=1505, 92) | -3.46 (± 1.43) | -3.59 (± 1.32) | | |

| | | | | |
|-----------------------|----------------|-----------------|--|--|
| Week 120 (n=1443, 88) | -3.49 (± 1.45) | -3.72 (± 1.20) | | |
| Week 144 (n=1381, 83) | -3.51 (± 1.41) | -3.79 (± 1.29) | | |
| Week 168 (n=1309, 81) | -3.52 (± 1.45) | -3.66 (± 1.30) | | |
| Week 192 (n=1250, 76) | -3.55 (± 1.43) | -3.61 (± 1.48) | | |
| Week 216 (n=1175, 73) | -3.59 (± 1.43) | -3.71 (± 1.24) | | |
| Week 240 (n=1118, 73) | -3.57 (± 1.44) | -3.90 (± 1.35) | | |
| Week 264 (n=1036, 62) | -3.64 (± 1.39) | -3.92 (± 1.36) | | |
| Week 288 (n=715, 26) | -3.80 (± 1.38) | -4.38 (± 1.33) | | |
| Week 312 (n=655, 7) | -3.86 (± 1.34) | -5.62 (± 0.86) | | |
| Week 336 (n=540, 0) | -3.86 (± 1.34) | 99999 (± 99999) | | |
| Week 360 (n=424, 0) | -3.93 (± 1.34) | 99999 (± 99999) | | |
| Week 384 (n=334, 0) | -3.99 (± 1.36) | 99999 (± 99999) | | |
| Week 408 (n=199, 0) | -3.85 (± 1.44) | 99999 (± 99999) | | |
| Week 432 (n=106, 0) | -4.11 (± 1.35) | 99999 (± 99999) | | |
| Week 456 (n=55, 0) | -4.01 (± 1.14) | 99999 (± 99999) | | |
| Week 480 (n=39, 0) | -3.69 (± 1.47) | 99999 (± 99999) | | |
| Week 504 (n=26, 0) | -3.76 (± 1.24) | 99999 (± 99999) | | |
| Week 516 (n=2, 0) | -3.76 (± 2.32) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Scores at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| | |
|-----------------|--|
| End point title | Change From Baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) Scores at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 |
|-----------------|--|

End point description:

HAQ-DI: standardised questionnaire used to assess degree of difficulty a subject has experienced during past week in 8 domains of daily living activities: dressing/grooming; arising; eating; walking; hygiene; reach; grip and activities. Total of 30 items distributed in these 8 domains. Each item was scored on 4-point scale from 0 to 3, where 0=no difficulty in physical function; 1=some difficulty in physical function; 2=much difficulty in physical function; 3=unable to do. Overall score was computed as sum of domain scores and divided by number of domains answered. Total possible score range 0 (least difficulty in physical function) to 3 (extreme difficulty in physical function), where higher scores=more difficulty while performing daily living activities. Baseline refers to Baseline of initial studies (EFC11072, ACT11575, EFC10832, SFY13370 and EFC13752). Safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and 'n' = subjects with available data.

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

End point timeframe:

Baseline, Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + Disease Modifying Anti- Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|--------------------------------------|--|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1895 | 111 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1895, 111) | -0.56 (± 0.63) | -0.58 (± 0.59) | | |
| Week 4 (n=1882, 109) | -0.59 (± 0.62) | -0.57 (± 0.52) | | |
| Week 8 (n=1858, 106) | -0.63 (± 0.63) | -0.63 (± 0.53) | | |
| Week 12 (n=1826, 109) | -0.65 (± 0.64) | -0.65 (± 0.57) | | |
| Week 24 (n=1787, 109) | -0.69 (± 0.65) | -0.63 (± 0.60) | | |
| Week 36 (n=1728, 109) | -0.70 (± 0.66) | -0.67 (± 0.61) | | |
| Week 48 (n=1667, 107) | -0.70 (± 0.66) | -0.63 (± 0.60) | | |
| Week 60 (n=1625, 103) | -0.70 (± 0.67) | -0.67 (± 0.50) | | |
| Week 72 (n=1586, 101) | -0.71 (± 0.66) | -0.67 (± 0.59) | | |
| Week 84 (n=1551, 95) | -0.71 (± 0.68) | -0.68 (± 0.59) | | |
| Week 96 (n=1509, 92) | -0.72 (± 0.67) | -0.69 (± 0.58) | | |
| Week 120 (n=1458, 89) | -0.74 (± 0.69) | -0.67 (± 0.55) | | |
| Week 144 (n=1386, 84) | -0.73 (± 0.70) | -0.64 (± 0.61) | | |
| Week 168 (n=1327, 81) | -0.74 (± 0.70) | -0.61 (± 0.59) | | |
| Week 192 (n=1268, 77) | -0.74 (± 0.71) | -0.65 (± 0.65) | | |
| Week 216 (n=1185, 70) | -0.75 (± 0.71) | -0.62 (± 0.69) | | |
| Week 240 (n=1127, 74) | -0.74 (± 0.72) | -0.61 (± 0.64) | | |
| Week 264 (n=998, 57) | -0.76 (± 0.71) | -0.54 (± 0.62) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Van Der Heijde Modified Total Sharp Score (mTSS) at Week 0 and Week 48 of LTS11210: Campaign 1 X-ray Data - Subjects From EFC11072 Part B

| | |
|-----------------|---|
| End point title | Change From Baseline in Van Der Heijde Modified Total Sharp Score (mTSS) at Week 0 and Week 48 of LTS11210: Campaign 1 X-ray Data - Subjects From EFC11072 Part B |
|-----------------|---|

End point description:

Van der Heijde modified Sharp method is composite X-ray scoring system used to assess structural (joint) disease progression (DP) in RA. The method evaluates both joint erosions (JE) for 44 joints and joint space narrowing (JSN) for 42 joints in bilateral hand and foot joints. Total mTSS: sum of the scores from both erosion score and joint space narrowing score and ranged from 0 (normal, no progression) to 448 (worst possible total score). An increase in total score represents progression of structural damage. Here, Baseline refers to the Baseline of initial study (EFC11072 Part B). In this endpoint, change from initial study baseline (CFISB) in 2 years X-ray data at Week 0 and 48 of LTS11210 were reported. Here, 'number of subjects analysed' = subjects from studies EFC11072 Part B evaluable for this endpoint and 'n'=subjects with available data. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

| | |
|-------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 0 and 48 of LTS11210 | |

| | | | | |
|--------------------------------------|------------------------------------|--|--|--|
| End point values | Sarilumab + DMARD: EFC11072 Part B | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 856 | | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 0 (n=856) | 1.05 (± 4.61) | | | |
| Change at Week 48 (n=848) | 1.34 (± 5.31) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Van Der Heijde Modified Total Sharp Score (mTSS) at Week 48 and Week 96 of LTS11210: Campaign 2 X-ray Data - Subjects From EFC11072 Part B

| | |
|-----------------|--|
| End point title | Change From Baseline in Van Der Heijde Modified Total Sharp Score (mTSS) at Week 48 and Week 96 of LTS11210: Campaign 2 X-ray Data - Subjects From EFC11072 Part B |
|-----------------|--|

End point description:

Van der Heijde modified Sharp method: composite X-ray scoring system to assess structural (joint) disease progression in RA. Method evaluates both JE for 44 joints and JSN for 42 joints in bilateral hand and foot joints. Total mTSS: sum of scores from both erosion score and joint space narrowing score and ranged from 0 (normal, no progression) to 448 (worst possible total score). Increase in total score=progression of structural damage. Baseline=Baseline of initial study (EFC11072 Part B). In this endpoint, CFISB in 3 years X-ray data (subjects with study duration of more than 48 weeks in LTS11210) at Week 48 and 96 from Campaign 2 were reported. Analysed on subset of subjects who previously completed study EFC11072, Part B with end of treatment X-ray evaluation. Number of subject analysed=subjects from study EFC11072 Part B evaluable for this endpoint and 'n'=subjects with available data. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm.

| | |
|--------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 48 and 96 of LTS11210 | |

| | | | | |
|--------------------------------------|------------------------------------|--|--|--|
| End point values | Sarilumab + DMARD: EFC11072 Part B | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 756 | | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |

| | | | | |
|---------------------------|---------------|--|--|--|
| Change at Week 48 (n=756) | 1.60 (± 5.96) | | | |
| Change at Week 96 (n=755) | 2.14 (± 7.20) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Van Der Heijde Modified Total Sharp Score (mTSS) at Week 96, 144 and Week 192 of LTS11210: Campaign 3 X-ray Data - Subjects From EFC11072 Part B

| | |
|-----------------|--|
| End point title | Change From Baseline in Van Der Heijde Modified Total Sharp Score (mTSS) at Week 96, 144 and Week 192 of LTS11210: Campaign 3 X-ray Data - Subjects From EFC11072 Part B |
|-----------------|--|

End point description:

Van der Heijde modified Sharp method: composite X-ray scoring system to assess structural (joint) disease progression in RA. Method evaluates both JE for 44 joints and JSN for 42 joints in bilateral hand and foot joints. Total mTSS: sum of scores from both erosion score and joint space narrowing score and ranged from 0 (normal, no progression) to 448 (worst possible total score). Increase in total score = progression of structural damage. Baseline = Baseline of initial study (EFC11072 Part B). In this endpoint, CFISB in 5 years X-ray data (subjects with study duration of more than 96 weeks in LTS11210) at Week 96, 144 and 192 from Campaign 3 were reported. Analysed on subset of subjects who previously completed study EFC11072, Part B with end of treatment X-ray evaluation. Number of subjects analysed = subjects from studies EFC11072 Part B evaluable for this endpoint and 'n' = subjects with data. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm.

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

End point timeframe:

Baseline, Week 96, 144 and 192 of LTS11210

| | | | | |
|--------------------------------------|------------------------------------|--|--|--|
| End point values | Sarilumab + DMARD: EFC11072 Part B | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 699 | | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change at Week 96 (n=699) | 1.83 (± 7.76) | | | |
| Change at Week 144 (n=689) | 2.24 (± 8.43) | | | |
| Change at Week 192 (n=656) | 2.83 (± 9.42) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With no Radiographic Progression of the Van Der Heijde Modified Total Sharp Score at Week 0 and 48 of LTS11210: Campaign 1 X-ray Data - Subjects From EFC11072 Part B

| | |
|--|--|
| End point title | Percentage of Subjects With no Radiographic Progression of the Van Der Heijde Modified Total Sharp Score at Week 0 and 48 of LTS11210: Campaign 1 X-ray Data - Subjects From EFC11072 Part B |
| End point description: | |
| Radiographic no progression: defined as a change from Baseline in Van der Heijde mTSS \leq 0. Van der Heijde modified Sharp method is composite X-ray scoring system to assess structural (joint) disease progression in RA. Method evaluates both JE for 44 joints and JSN for 42 joints in bilateral hand and foot joints. Total mTSS = sum of scores from both erosion score and joint space narrowing score, ranged from 0 (normal, no progression) to 448 (worst possible total score). Increase in total score = progression of structural damage. In this endpoint, percentage (%) of subjects with no radiographic progression at Week 48 of LTS11210 from Campaign 1 X-ray data were reported. Analysed on subset of subjects who previously completed study EFC11072, Part B with end of treatment X-ray evaluation. Here, 'number of subjects analysed'=subjects from studies EFC11072 Part B evaluable for this endpoint. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 0 (post-dose) and 48 of LTS11210 | |

| End point values | Sarilumab + DMARD: EFC11072 Part B | | | |
|-------------------------------|------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 889 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 0 | 51.9 | | | |
| Week 48 | 51.2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With no Radiographic Progression of the Van Der Heijde Modified Total Sharp Score at Week 48 and 96 of LTS11210: Campaign 2 X-ray Data - Subjects From EFC11072 Part B

| | |
|--|---|
| End point title | Percentage of Subjects With no Radiographic Progression of the Van Der Heijde Modified Total Sharp Score at Week 48 and 96 of LTS11210: Campaign 2 X-ray Data - Subjects From EFC11072 Part B |
| End point description: | |
| Radiographic no progression: defined as change from Baseline in Van der Heijde mTSS \leq 0. Van der Heijde modified Sharp method: composite X-ray scoring system to assess structural (joint) DP in RA. Method evaluates both JE for 44 joints and JSN for 42 joints in bilateral hand and foot joints. Total mTSS = sum of scores from erosion score and joint space narrowing score, ranged from 0 (normal, no progression) to 448 (worst possible total score). Increase in total score = progression of structural damage. In this endpoint, % of subjects with no radiographic progression at Week 48 and 96 of LTS11210 from Campaign 2 X-ray data (subjects with study duration of more than 48 weeks in LTS11210) were reported. Analysed on subset of subjects who previously completed study EFC11072, Part B with end of treatment X-ray evaluation. Number of subjects analysed = subjects from study EFC11072 Part B evaluable for this endpoint. Data for this endpoint was not planned to be collected for Sarilumab Monotherapy arm. | |
| End point type | Secondary |

End point timeframe:

Week 48 and 96 of LTS11210

| End point values | Sarilumab + DMARD: EFC11072 Part B | | | |
|-------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 796 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 48 | 46.6 | | | |
| Week 96 | 44.2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With no Radiographic Progression of the Van Der Heijde Modified Total Sharp Score at Week 96, 144 and 192 of LTS11210: Campaign 3 X-ray Data - Subjects From EFC11072 Part B

| | |
|-----------------|---|
| End point title | Percentage of Subjects With no Radiographic Progression of the Van Der Heijde Modified Total Sharp Score at Week 96, 144 and 192 of LTS11210: Campaign 3 X-ray Data - Subjects From EFC11072 Part B |
|-----------------|---|

End point description:

Radiographic no progression: defined as change from Baseline in Van der Heijde mTSS ≤ 0 . Van der Heijde modified Sharp method: composite X-ray scoring system used to assess structural (joint) DP in RA. Method evaluates both JE for 44 joints and JSN for 42 joints in bilateral hand and foot joints. Total mTSS: sum of scores from erosion score and joint space narrowing score, ranged: 0 (normal, no progression) to 448 (worst possible total score). Increase in total score = progression of structural damage. In this endpoint % of subjects with no radiographic progression at Week 96, 144 and 192 from Campaign 3 X-ray data (subjects with study duration more than 96 weeks in LTS11210) were reported. Analysed on subset of subjects who previously completed study EFC11072, Part B with end of treatment X-ray evaluation. Number of subjects analysed = subjects from studies EFC11072 Part B evaluable for endpoint. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm.

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

End point timeframe:

Week 96, 144 and 192 of LTS11210

| End point values | Sarilumab + DMARD: EFC11072 Part B | | | |
|-------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 732 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

| | | | | |
|----------|------|--|--|--|
| Week 96 | 48.6 | | | |
| Week 144 | 46.0 | | | |
| Week 192 | 41.8 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tender Joint Count (TJC) at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| | |
|-----------------|---|
| End point title | Change From Baseline in Tender Joint Count (TJC) at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210 |
|-----------------|---|

End point description:

TJC is the sum of all tender joints based on examination of the 68 joints of the fingers, elbows, hips, knees, ankles, and toes. Total TJC ranged from 0 (best) to 68 (worst), where higher score = more severity. Change from Baseline in TJC was reported in the endpoint. Here, Baseline refers to Baseline of initial study (EFC11072, ACT11575, EFC10832, SFY13370 and EFC13752). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and 'n' = subjects with available data for each specified category and "99999" was used as space filler which indicates that data was not planned to be collected and analysed for the specified time-points in the respective groups.

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

End point timeframe:

Baseline, Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| End point values | Sarilumab + Disease Modifying Anti- Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|--------------------------------------|--|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1904 | 111 | | |
| Units: joints | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1904, 111) | -16.67 (± 14.05) | -19.86 (± 12.43) | | |
| Week 4 (n=1891, 109) | -18.97 (± 13.81) | -20.13 (± 12.64) | | |
| Week 8 (n=1867, 106) | -19.72 (± 13.61) | -20.09 (± 11.73) | | |
| Week 12 (n=1837, 109) | -20.20 (± 13.89) | -20.05 (± 12.99) | | |
| Week 24 (n=1791, 109) | -20.67 (± 14.09) | -21.19 (± 12.55) | | |
| Week 36 (n=1733, 109) | -20.68 (± 14.39) | -20.60 (± 12.19) | | |
| Week 48 (n=1674, 107) | -20.95 (± 14.04) | -20.27 (± 13.54) | | |

| | | | | |
|-----------------------|------------------|------------------|--|--|
| Week 60 (n=1625, 103) | -21.29 (± 14.06) | -20.95 (± 12.66) | | |
| Week 72 (n=1589, 101) | -21.41 (± 13.98) | -21.67 (± 12.65) | | |
| Week 84 (n=1553, 95) | -21.53 (± 14.17) | -21.36 (± 13.04) | | |
| Week 96 (n=1514, 92) | -21.65 (± 14.08) | -20.89 (± 13.50) | | |
| Week 120 (n=1459, 88) | -21.92 (± 14.20) | -20.18 (± 12.73) | | |
| Week 144 (n=1394, 83) | -22.13 (± 14.01) | -22.52 (± 13.41) | | |
| Week 168 (n=1331, 81) | -22.35 (± 14.26) | -22.42 (± 13.34) | | |
| Week 192 (n=1269, 78) | -22.62 (± 14.20) | -21.83 (± 13.79) | | |
| Week 216 (n=1211, 76) | -22.69 (± 14.28) | -22.33 (± 13.29) | | |
| Week 240 (n=1136, 74) | -22.89 (± 14.47) | -23.07 (± 14.24) | | |
| Week 264 (n=1072, 62) | -23.09 (± 14.08) | -23.66 (± 15.02) | | |
| Week 288 (n=788, 26) | -22.59 (± 15.70) | -28.95 (± 14.79) | | |
| Week 312 (n=713, 7) | -23.47 (± 15.23) | -43.71 (± 12.12) | | |
| Week 336 (n=556, 0) | -23.37 (± 15.24) | 99999 (± 99999) | | |
| Week 360 (n=442, 0) | -24.12 (± 14.89) | 99999 (± 99999) | | |
| Week 384 (n=358, 0) | -24.73 (± 15.14) | 99999 (± 99999) | | |
| Week 408 (n=226, 0) | -24.58 (± 14.97) | 99999 (± 99999) | | |
| Week 432 (n=109, 0) | -25.33 (± 15.05) | 99999 (± 99999) | | |
| Week 456 (n=59, 0) | -24.21 (± 14.37) | 99999 (± 99999) | | |
| Week 480 (n=45, 0) | -21.23 (± 14.66) | 99999 (± 99999) | | |
| Week 504 (n=27, 0) | -23.62 (± 13.63) | 99999 (± 99999) | | |
| Week 516 (n=2, 0) | -24.00 (± 12.73) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Swollen Joint Count (SJC) at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| | |
|-----------------|--|
| End point title | Change From Baseline in Swollen Joint Count (SJC) at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210 |
|-----------------|--|

End point description:

SJC is the sum of all swollen joints based on examination of the fingers, elbows, knees and toes. Total

SJC ranged from 0 (best) to 66 (worst), where higher score = more severity. Change from Baseline in SJC was reported in the endpoint. Here, Baseline refers to the Baseline of initial studies (EFC11072, ACT11575, EFC10832, SFY13370 and EFC13752). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and 'n' = subject with available data for each specified category and "99999" was used as space filler which indicates that data was not planned to be collected and analysed for the specified time-points in the respective groups.

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

End point timeframe:

Baseline, Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| End point values | Sarilumab + Disease Modifying Anti- Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|--------------------------------------|--|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1904 | 111 | | |
| Units: joints | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1904, 111) | -11.36 (± 9.96) | -14.06 (± 9.65) | | |
| Week 4 (n=1891, 109) | -12.81 (± 9.77) | -14.55 (± 9.19) | | |
| Week 8 (n=1867, 106) | -13.43 (± 9.82) | -14.60 (± 9.30) | | |
| Week 12 (n=1837, 109) | -13.77 (± 10.13) | -14.58 (± 9.31) | | |
| Week 24 (n=1791, 109) | -14.28 (± 10.09) | -14.83 (± 9.64) | | |
| Week 36 (n=1733, 109) | -14.37 (± 9.99) | -14.51 (± 9.70) | | |
| Week 48 (n=1674, 107) | -14.53 (± 9.97) | -14.96 (± 9.22) | | |
| Week 60 (n=1625, 103) | -14.75 (± 10.20) | -15.54 (± 9.49) | | |
| Week 72 (n=1589, 101) | -14.76 (± 10.12) | -15.43 (± 9.67) | | |
| Week 84 (n=1553, 95) | -14.84 (± 10.16) | -15.83 (± 9.50) | | |
| Week 96 (n=1514, 92) | -15.03 (± 10.20) | -15.51 (± 10.24) | | |
| Week 120 (n=1459, 88) | -15.09 (± 10.17) | -15.77 (± 9.95) | | |
| Week 144 (n=1394, 83) | -15.18 (± 10.20) | -15.90 (± 8.57) | | |
| Week 168 (n=1331, 81) | -15.16 (± 10.30) | -15.47 (± 8.91) | | |
| Week 192 (n=1269, 78) | -15.26 (± 10.09) | -15.01 (± 9.17) | | |
| Week 216 (n=1211, 76) | -15.25 (± 9.97) | -15.72 (± 8.65) | | |
| Week 240 (n=1135, 74) | -15.43 (± 10.34) | -15.59 (± 9.08) | | |
| Week 264 (n=1072, 62) | -15.50 (± 9.79) | -16.59 (± 9.53) | | |

| | | | | |
|----------------------|------------------|-----------------|--|--|
| Week 288 (n=788, 26) | -14.67 (± 10.98) | -18.65 (± 8.90) | | |
| Week 312 (n=713, 7) | -15.38 (± 10.71) | -23.57 (± 9.83) | | |
| Week 336 (n=556, 0) | -15.51 (± 10.48) | 99999 (± 99999) | | |
| Week 360 (n=442, 0) | -15.96 (± 10.76) | 99999 (± 99999) | | |
| Week 384 (n=358, 0) | -16.42 (± 10.76) | 99999 (± 99999) | | |
| Week 408 (n=226, 0) | -16.30 (± 11.47) | 99999 (± 99999) | | |
| Week 432 (n=109, 0) | -16.62 (± 11.51) | 99999 (± 99999) | | |
| Week 456 (n=59, 0) | -15.64 (± 10.65) | 99999 (± 99999) | | |
| Week 480 (n=45, 0) | -15.43 (± 10.67) | 99999 (± 99999) | | |
| Week 504 (n=27, 0) | -16.21 (± 10.94) | 99999 (± 99999) | | |
| Week 516 (n=2, 0) | -13.00 (± 2.83) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physician's Global Assessments of Disease Activity Visual Analogue Scale (VAS) Score at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, and 264 of LTS11210

| | |
|-----------------|---|
| End point title | Change From Baseline in Physician's Global Assessments of Disease Activity Visual Analogue Scale (VAS) Score at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, and 264 of LTS11210 |
|-----------------|---|

End point description:

Physician global assessment of disease activity was measured on a 100 millimetres (mm) horizontal VAS, ranging from 0 (best disease activity) to 100 (worst disease activity), where lower score = less disease activity and higher score = more disease activity. Here, Baseline refers to Baseline of initial studies (EFC11072, ACT11575, EFC10832, SFY13370 and EFC13752). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and 'n' = subjects with available data for each specified category.

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

End point timeframe:

Baseline, Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, and 264 of LTS11210

| | | | | |
|-----------------------------|--|-----------------------|--|--|
| End point values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1903 | 110 | | |

| | | | | |
|--------------------------------------|------------------|------------------|--|--|
| Units: millimetres | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1903, 110) | -40.51 (± 23.82) | -46.38 (± 19.17) | | |
| Week 4 (n=1888, 109) | -43.98 (± 22.03) | -47.94 (± 19.16) | | |
| Week 8 (n=1863, 106) | -45.79 (± 22.06) | -49.27 (± 18.80) | | |
| Week 12 (n=1832, 109) | -47.02 (± 22.03) | -50.20 (± 19.74) | | |
| Week 24 (n=1786, 109) | -48.39 (± 21.94) | -50.82 (± 19.99) | | |
| Week 36 (n=1730, 109) | -48.94 (± 21.72) | -51.12 (± 19.87) | | |
| Week 48 (n=1675, 107) | -49.36 (± 21.68) | -50.58 (± 21.38) | | |
| Week 60 (n=1624, 103) | -49.98 (± 21.62) | -51.40 (± 20.51) | | |
| Week 72 (n=1586, 101) | -49.91 (± 21.72) | -52.90 (± 19.40) | | |
| Week 84 (n=1551, 94) | -50.28 (± 21.42) | -55.84 (± 17.39) | | |
| Week 96 (n=1512, 92) | -50.73 (± 21.62) | -54.14 (± 18.97) | | |
| Week 120 (n=1458, 88) | -50.43 (± 21.39) | -54.33 (± 19.41) | | |
| Week 144 (n=1390, 84) | -50.84 (± 21.13) | -55.73 (± 18.04) | | |
| Week 168 (n=1329, 81) | -50.49 (± 21.65) | -53.21 (± 21.36) | | |
| Week 192 (n=1264, 78) | -50.32 (± 22.00) | -52.22 (± 22.44) | | |
| Week 216 (n=1209, 76) | -51.49 (± 21.57) | -54.67 (± 18.30) | | |
| Week 240 (n=1133, 74) | -51.00 (± 21.57) | -55.16 (± 18.82) | | |
| Week 264 (n=1055, 63) | -51.18 (± 21.24) | -55.27 (± 21.70) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subject Global Assessment of Disease Activity Visual Analogue Scale Score at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210

| | |
|-----------------|--|
| End point title | Change From Baseline in Subject Global Assessment of Disease Activity Visual Analogue Scale Score at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210 |
|-----------------|--|

End point description:

Subject global assessment of disease activity was measured on a 100 mm horizontal VAS, ranging from 0 (best disease activity) to 100 (worst disease activity), where lower score = less disease activity and higher score = more disease activity. Here, Baseline refers to the Baseline of initial studies (EFC11072, ACT11575, EFC10832, SFY13370 and EFC13752). Analysis was performed on safety population. Here, number of subjects analysed' = subjects evaluable for endpoint and 'n' = subject with available data for

each specified category and "99999" was used as space filler which indicates that data was not planned to be collected and analysed for the specified time-points in the respective groups.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, 264, 288, 312, 336, 360, 384, 408, 432, 456, 480, 504 and 516 of LTS11210 | |

| End point values | Sarilumab + Disease Modifying Anti- Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|--------------------------------------|--|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1904 | 111 | | |
| Units: millimetres | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1904, 111) | -30.51 (± 26.78) | -32.30 (± 27.55) | | |
| Week 4 (n=1887, 109) | -32.87 (± 25.60) | -33.63 (± 25.86) | | |
| Week 8 (n=1863, 106) | -34.65 (± 26.25) | -34.25 (± 25.90) | | |
| Week 12 (n=1830, 109) | -35.60 (± 26.77) | -34.24 (± 28.38) | | |
| Week 24 (n=1785, 109) | -36.91 (± 26.50) | -36.12 (± 27.82) | | |
| Week 36 (n=1729, 109) | -37.08 (± 27.18) | -37.13 (± 24.73) | | |
| Week 48 (n=1674, 107) | -37.28 (± 26.93) | -35.98 (± 28.18) | | |
| Week 60 (n=1622, 103) | -37.79 (± 27.38) | -37.82 (± 25.40) | | |
| Week 72 (n=1589, 101) | -37.90 (± 27.26) | -37.95 (± 26.53) | | |
| Week 84 (n=1552, 95) | -37.45 (± 27.82) | -40.52 (± 26.69) | | |
| Week 96 (n=1512, 92) | -38.34 (± 27.34) | -41.46 (± 26.57) | | |
| Week 120 (n=1459, 89) | -38.41 (± 27.43) | -41.67 (± 26.43) | | |
| Week 144 (n=1394, 84) | -38.91 (± 27.52) | -38.52 (± 26.40) | | |
| Week 168 (n=1328, 81) | -38.22 (± 28.26) | -37.27 (± 27.46) | | |
| Week 192 (n=1267, 76) | -39.26 (± 28.16) | -37.79 (± 32.12) | | |
| Week 216 (n=1191, 74) | -39.96 (± 27.72) | -38.72 (± 32.76) | | |
| Week 240 (n=1133, 74) | -39.54 (± 27.79) | -41.64 (± 30.13) | | |
| Week 264 (n=1061, 62) | -39.87 (± 27.31) | -37.84 (± 32.94) | | |
| Week 288 (n=727, 26) | -43.68 (± 25.55) | -48.00 (± 33.87) | | |
| Week 312 (n=671, 7) | -44.05 (± 26.40) | -65.71 (± 21.40) | | |

| | | | | |
|---------------------|------------------|-----------------|--|--|
| Week 336 (n=543, 0) | -43.42 (± 26.95) | 99999 (± 99999) | | |
| Week 360 (n=445, 0) | -44.56 (± 26.59) | 99999 (± 99999) | | |
| Week 384 (n=349, 0) | -47.19 (± 26.25) | 99999 (± 99999) | | |
| Week 408 (n=214, 0) | -44.97 (± 29.16) | 99999 (± 99999) | | |
| Week 432 (n=109, 0) | -49.77 (± 25.95) | 99999 (± 99999) | | |
| Week 456 (n=58, 0) | -50.40 (± 24.27) | 99999 (± 99999) | | |
| Week 480 (n=43, 0) | -46.65 (± 29.66) | 99999 (± 99999) | | |
| Week 504 (n=27, 0) | -48.89 (± 28.83) | 99999 (± 99999) | | |
| Week 516 (n=2,0) | -40.50 (± 36.06) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subject's Assessment of Pain Visual Analogue Scale Score at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, and 264 of LTS11210

| | |
|-----------------|---|
| End point title | Change From Baseline in Subject's Assessment of Pain Visual Analogue Scale Score at Week 0, 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, and 264 of LTS11210 |
|-----------------|---|

End point description:

Subjects were requested to indicate their pain intensity due to their RA on a 100 mm horizontal VAS, ranging from 0 (no pain) to 100 (worst pain), where a higher score represented more pain due to RA. Here, Baseline refers to the Baseline of initial studies (EFC11072, ACT11575, EFC10832, SFY13370 and EFC13752). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects evaluable for endpoint and 'n' = subjects with available data for each specified category.

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

End point timeframe:

Baseline, Week 0 (post-dose), 4, 8, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240, and 264 of LTS11210

| End point values | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | | |
|--------------------------------------|--|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1897 | 111 | | |
| Units: millimetres | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1897, 111) | -31.08 (± 27.45) | -37.01 (± 28.73) | | |
| Week 4 (n=1885, 109) | -34.04 (± 26.52) | -37.53 (± 27.28) | | |

| | | | | |
|-----------------------|------------------|------------------|--|--|
| Week 8 (n=1859, 106) | -35.79 (± 26.88) | -38.14 (± 27.16) | | |
| Week 12 (n=1827, 109) | -36.46 (± 27.46) | -39.08 (± 26.79) | | |
| Week 24 (n=1784, 109) | -37.87 (± 27.07) | -38.75 (± 28.12) | | |
| Week 36 (n=1725, 109) | -37.60 (± 27.97) | -39.56 (± 25.72) | | |
| Week 48 (n=1671, 107) | -38.07 (± 28.33) | -39.41 (± 30.12) | | |
| Week 60 (n=1621, 103) | -38.46 (± 28.18) | -40.79 (± 26.20) | | |
| Week 72 (n=1587, 101) | -38.00 (± 28.54) | -42.62 (± 27.33) | | |
| Week 84 (n=1547, 95) | -38.37 (± 28.79) | -42.38 (± 28.69) | | |
| Week 96 (n=1510, 92) | -38.62 (± 28.57) | -43.73 (± 27.59) | | |
| Week 120 (n=1457, 89) | -39.29 (± 28.44) | -44.11 (± 25.69) | | |
| Week 144 (n=1392, 84) | -39.19 (± 28.21) | -41.42 (± 27.31) | | |
| Week 168 (n=1325, 81) | -39.47 (± 28.84) | -38.86 (± 29.46) | | |
| Week 192 (n=1266, 76) | -40.17 (± 28.98) | -41.25 (± 30.44) | | |
| Week 216 (n=1185, 70) | -40.25 (± 28.56) | -44.01 (± 30.27) | | |
| Week 240 (n=1129, 74) | -40.28 (± 28.44) | -43.59 (± 29.22) | | |
| Week 264 (n=1044, 62) | -41.02 (± 28.09) | -40.71 (± 29.79) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Short Form 36 (SF-36; Version 2) Physical Component Summary (PCS) Score at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, ACT11575 and EFC10832 Only

| | |
|-----------------|--|
| End point title | Change From Baseline in Short Form 36 (SF-36; Version 2) Physical Component Summary (PCS) Score at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, ACT11575 and EFC10832 Only |
|-----------------|--|

End point description:

SF-36 is a generic 36-item questionnaire consisting of 8 domains, measuring quality of life (QoL) covering 2 summary measures: PCS and mental component summary (MCS). PCS with 4 domains: physical functioning, role limitations due to physical problems, bodily pain, and general health; and MCS with 4 domains: vitality, social functioning, role limitations due to emotional problems, and mental health. Each domain is scored by summing individual items, which are transformed into a score range from 0 to 100; where 0=worst QoL to 100=best QoL. PCS total score ranged from 0 to 100 with higher scores = better physical health. Here, Baseline refers to Baseline of initial studies (EFC11072, ACT11575 and EFC10832). Here, 'number of subjects analysed'=subjects from studies EFC11072, ACT11575 and EFC10832 evaluable for this endpoint and 'n'=subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm.

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

End point timeframe:

Baseline, Week 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC11072, ACT11575 and EFC10832 | | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1367 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1301) | 7.95 (± 8.29) | | | |
| Week 12 (n=1367) | 8.84 (± 8.45) | | | |
| Week 24 (n=1339) | 9.25 (± 8.59) | | | |
| Week 36 (n=1303) | 9.72 (± 8.85) | | | |
| Week 48 (n=1269) | 9.43 (± 8.89) | | | |
| Week 60 (n=1231) | 9.64 (± 8.53) | | | |
| Week 72 (n=1213) | 9.62 (± 8.78) | | | |
| Week 84 (n=1179) | 9.95 (± 8.97) | | | |
| Week 96 (n=1143) | 9.90 (± 8.90) | | | |
| Week 120 (n=1111) | 10.18 (± 9.12) | | | |
| Week 144 (n=1065) | 10.15 (± 9.18) | | | |
| Week 168 (n=1018) | 10.24 (± 9.24) | | | |
| Week 192 (n=967) | 10.34 (± 9.52) | | | |
| Week 216 (n=908) | 10.15 (± 9.45) | | | |
| Week 240 (n=848) | 10.38 (± 9.21) | | | |
| Week 264 (n=754) | 10.32 (± 9.38) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Short Form 36 (SF-36; Version 2) Mental Component Summary Score at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, ACT11575 and EFC10832 Only

| | |
|-----------------|--|
| End point title | Change From Baseline in Short Form 36 (SF-36; Version 2) Mental Component Summary Score at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, ACT11575 and EFC10832 Only |
|-----------------|--|

End point description:

SF-36 is a generic 36-item questionnaire consisting of 8 domains, measuring QoL covering 2 summary measures: PCS and MCS. PCS with 4 domains: physical functioning, role limitations due to physical problems, bodily pain and general health; and MCS with 4 domains: vitality, social functioning, role limitations due to emotional problems and mental health. Each domain is scored by summing the individual items, which are transformed into a score range from 0 to 100; 0 = worst QoL to 100 = best QoL. MCS total score ranged from 0 to 100 with higher scores = better physical and mental health. Here, Baseline refers to the Baseline of initial studies (EFC11072, ACT11575 and EFC10832). Analysed

on safety population. Here, 'number of subjects analysed'=subjects from studies EFC11072, ACT11575 and EFC10832 evaluable for this endpoint and 'n'=subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 | |

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Sarilumab + DMARD: EFC11072, ACT11575 and EFC10832 | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1367 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1301) | 6.43 (± 10.80) | | | |
| Week 12 (n=1367) | 7.15 (± 11.03) | | | |
| Week 24 (n=1339) | 7.43 (± 11.15) | | | |
| Week 36 (n=1303) | 7.20 (± 11.31) | | | |
| Week 48 (n=1269) | 7.48 (± 11.15) | | | |
| Week 60 (n=1231) | 7.43 (± 11.21) | | | |
| Week 72 (n=1213) | 7.25 (± 11.24) | | | |
| Week 84 (n=1179) | 7.29 (± 11.20) | | | |
| Week 96 (n=1143) | 7.47 (± 11.52) | | | |
| Week 120 (n=1111) | 7.69 (± 11.62) | | | |
| Week 144 (n=1065) | 7.22 (± 11.60) | | | |
| Week 168 (n=1018) | 7.29 (± 11.52) | | | |
| Week 192 (n=967) | 7.10 (± 11.51) | | | |
| Week 216 (n=908) | 7.20 (± 11.91) | | | |
| Week 240 (n=848) | 7.23 (± 12.03) | | | |
| Week 264 (n=754) | 7.32 (± 12.08) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-fatigue) Total Score at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, ACT11575 and EFC10832 only

| | |
|-----------------|---|
| End point title | Change From Baseline in Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-fatigue) Total Score at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, ACT11575 and EFC10832 only |
|-----------------|---|

End point description:

The FACIT-F is a 13-item questionnaire assessing fatigue where subjects scored each item on a 5-point scale (0 to 4): 0=not at all, 1=a little bit, 2=somewhat, 3=quite a bit, 4=very much. The sum of all

responses resulted in the FACIT-Fatigue total score ranged from 0 to 52, where higher score = lower level of fatigue and indicates better QoL. A positive change from baseline score indicates an improvement. Here, Baseline refers to the Baseline of initial studies (EFC11072, ACT11575, and EFC10832). Here, 'number of subjects analysed' = subjects from studies EFC11072, ACT11575 and EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 | |

| End point values | Sarilumab + DMARD: EFC11072, ACT11575 and EFC10832 | | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1651 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=1342) | 9.20 (± 10.05) | | | |
| Week 12 (n=1651) | 10.26 (± 10.10) | | | |
| Week 24 (n=1621) | 10.94 (± 10.31) | | | |
| Week 36 (n=1570) | 10.91 (± 10.67) | | | |
| Week 48 (n=1520) | 10.86 (± 10.64) | | | |
| Week 60 (n=1474) | 10.97 (± 10.50) | | | |
| Week 72 (n=1444) | 10.84 (± 10.68) | | | |
| Week 84 (n=1411) | 10.75 (± 10.88) | | | |
| Week 96 (n=1372) | 11.09 (± 10.85) | | | |
| Week 120 (n=1323) | 11.18 (± 10.74) | | | |
| Week 144 (n=1262) | 11.14 (± 10.86) | | | |
| Week 168 (n=1197) | 11.00 (± 11.27) | | | |
| Week 192 (n=1141) | 10.80 (± 11.10) | | | |
| Week 216 (n=1062) | 11.12 (± 11.25) | | | |
| Week 240 (n=1013) | 11.15 (± 11.21) | | | |
| Week 264 (n=910) | 10.99 (± 11.19) | | | |

Statistical analyses

Secondary: Change From Baseline in Sleep Visual Analogue Scale Score at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, and ACT11575 only

| | |
|-----------------|---|
| End point title | Change From Baseline in Sleep Visual Analogue Scale Score at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, and ACT11575 only |
|-----------------|---|

End point description:

Rheumatoid arthritis (RA), like other chronic illness, is associated with sleep disturbances and is linked to pain, mood, and disease activity. The effect of sarilumab on sleep was assessed on a on 100 mm horizontal VAS scale, ranging from 0 (sleep is not a problem) to 100 (sleep is a major problem), where higher score = more sleep disturbances. Here, Baseline refers to the Baseline of initial studies (EFC11072, and ACT11575). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from studies EFC11072, and ACT11575 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

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

End point timeframe:

Baseline, Week 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC11072, and ACT11575 | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1231 | | | |
| Units: millimetres | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=894) | -24.58 (± 30.96) | | | |
| Week 12 (n=1231) | -26.11 (± 30.59) | | | |
| Week 24 (n=1206) | -26.44 (± 30.94) | | | |
| Week 36 (n=1164) | -27.37 (± 31.52) | | | |
| Week 48 (n=1132) | -26.15 (± 31.37) | | | |
| Week 60 (n=1098) | -26.98 (± 31.24) | | | |
| Week 72 (n=1075) | -26.85 (± 32.16) | | | |
| Week 84 (n=1051) | -25.81 (± 31.90) | | | |
| Week 96 (n=1024) | -26.91 (± 31.63) | | | |
| Week 120 (n=983) | -27.63 (± 32.26) | | | |
| Week 144 (n=940) | -26.90 (± 31.54) | | | |
| Week 168 (n=892) | -27.33 (± 33.25) | | | |
| Week 192 (n=853) | -26.87 (± 32.03) | | | |

| | | | | |
|------------------|------------------|--|--|--|
| Week 216 (n=802) | -28.58 (± 31.46) | | | |
| Week 240 (n=755) | -27.72 (± 33.07) | | | |
| Week 264 (n=705) | -27.71 (± 32.08) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Work Productivity and Activity Impairment (WPAI): Percent Work Time Missed due to RA at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072 and ACT11575 only

| | |
|-----------------|---|
| End point title | Change From Baseline in Work Productivity and Activity Impairment (WPAI): Percent Work Time Missed due to RA at Week 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072 and ACT11575 only |
|-----------------|---|

End point description:

WPAI assesses work productivity and impairment. It is 6-item questionnaire to assess degree to which RA affected work productivity and regular activities over past 7 days. Questions were: Q1=currently employed; Q2=hours missed due to RA; Q3=hours missed due to other reasons; Q4=hours actually worked; Q5=RA affected productivity while working (0-10 scale, with higher numbers=less productivity); Q6=RA affected regular activities (0-10 scale, higher numbers=greater impairment). Percent work time missed due to RA was subscale and calculated: $100 \times Q2 / (Q2 + Q4)$ for those who were currently employed. Subscale score was expressed as impairment percentage (range:0 to 100%) where higher numbers=greater impairment and less productivity. Baseline=Baseline of initial studies (EFC11072 and ACT11575). Safety population. Number of subjects analysed=subjects from studies EFC11072 and ACT11575 evaluable for this endpoint & 'n'=with data. Data was not planned to be collected for Sarilumab Monotherapy arm.

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

End point timeframe:

Baseline, Week 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC11072, and ACT11575 | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 267 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=191) | -10.82 (± 30.64) | | | |
| Week 12 (n=267) | -8.62 (± 28.67) | | | |
| Week 24 (n=255) | -11.92 (± 29.33) | | | |
| Week 36 (n=251) | -9.62 (± 30.08) | | | |
| Week 48 (n=243) | -11.39 (± 29.92) | | | |

| | | | | |
|------------------|------------------|--|--|--|
| Week 60 (n=236) | -10.03 (± 25.74) | | | |
| Week 72 (n=216) | -9.10 (± 28.14) | | | |
| Week 84 (n=206) | -8.20 (± 27.06) | | | |
| Week 96 (n=209) | -11.32 (± 30.28) | | | |
| Week 120 (n=189) | -8.62 (± 32.95) | | | |
| Week 144 (n=183) | -9.01 (± 30.16) | | | |
| Week 168 (n=176) | -10.38 (± 31.48) | | | |
| Week 192 (n=166) | -8.99 (± 29.24) | | | |
| Week 216 (n=147) | -11.17 (± 29.35) | | | |
| Week 240 (n=147) | -8.57 (± 26.11) | | | |
| Week 264 (n=133) | -13.40 (± 30.57) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Work Productivity and Activity Impairment: Percent Impairment While Working due to RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, and ACT11575 only

| | |
|-----------------|--|
| End point title | Change From Baseline in Work Productivity and Activity Impairment: Percent Impairment While Working due to RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, and ACT11575 only |
|-----------------|--|

End point description:

WPAI assesses work productivity & impairment. It is 6-item questionnaire to assess degree to which RA affected work productivity & regular activities over past 7 days. Questions: Q1=currently employed; Q2=hours(hrs) missed due to RA; Q3=hrs missed due to other reasons; Q4=hrs actually worked; Q5=RA affected productivity while working (0-10 scale, higher numbers=less productivity); Q6=RA affected regular activities (0-10 scale, higher numbers=greater impairment). Percent impairment while working was subscale and calculated: $10 \times Q5$ for those who were currently employed & actually worked in past 7 days. Subscale score=expressed as impairment percentage (range:0-100%), where higher numbers=greater impairment and less productivity. Baseline:Baseline of initial studies (EFC11072 & ACT11575). Safety population. Number of subjects analysed=subjects from studies EFC11072 & ACT11575 evaluable for this endpoint and 'n'=with data. Data was not planned to be collected for Sarilumab monotherapy arm.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| | | | | |
|--------------------------------------|---|--|--|--|
| End point values | Sarilumab + DMARD: EFC11072, and ACT11575 | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 273 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=194) | -21.65 (± 27.74) | | | |
| Week 12 (n=273) | -22.16 (± 26.53) | | | |
| Week 24 (n=258) | -23.45 (± 26.70) | | | |
| Week 36 (n=254) | -27.01 (± 27.11) | | | |
| Week 48 (n=252) | -24.76 (± 26.05) | | | |
| Week 60 (n=240) | -25.17 (± 25.12) | | | |
| Week 72 (n=224) | -24.33 (± 27.57) | | | |
| Week 84 (n=214) | -24.02 (± 27.09) | | | |
| Week 96 (n=212) | -26.42 (± 27.11) | | | |
| Week 120 (n=189) | -24.02 (± 27.63) | | | |
| Week 144 (n=184) | -24.67 (± 28.20) | | | |
| Week 168 (n=181) | -24.25 (± 28.46) | | | |
| Week 192 (n=168) | -25.24 (± 26.60) | | | |
| Week 216 (n=147) | -24.56 (± 27.28) | | | |
| Week 240 (n=155) | -24.39 (± 26.48) | | | |
| Week 264 (n=135) | -25.26 (± 27.40) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Work Productivity and Activity Impairment: Percent Overall Work Impairment due to RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, and ACT11575 only

| | |
|-----------------|---|
| End point title | Change From Baseline in Work Productivity and Activity Impairment: Percent Overall Work Impairment due to RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, and ACT11575 only |
|-----------------|---|

End point description:

WPAI assesses work productivity and impairment. It is 6-item questionnaire to assess degree to which RA affected work productivity & regular activities over past 7 days. Questions were: Q1=currently employed; Q2=hrs missed due to RA; Q3=hrs missed due to other reasons;Q4=hrs actually worked;

Q5=RA affected productivity while working (0-10 scale, higher numbers=less productivity); Q6=RA affected regular activities (0-10 scale, higher numbers=greater impairment). Percent overall work impairment due to RA was subscale and calculated: $100 \times Q2 / (Q2 + Q4) + 100 \times [(1 - Q2 / (Q2 + Q4)) \times (Q5 / 10)]$ for those who were currently employed. Subscale score=expressed as impairment percentage (range:0-100%) where higher numbers=greater impairment. Baseline: Baseline of initial studies (EFC11072 and ACT11575). Safety population. Number of subjects analysed=subjects from studies EFC11072, and ACT11575 evaluable for this endpoint and 'n'=with data. Data was not planned to be collected for Sarilumab monotherapy arm.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC11072, and ACT11575 | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 246 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=172) | -22.84 (± 30.73) | | | |
| Week 12 (n=246) | -23.13 (± 27.98) | | | |
| Week 24 (n=232) | -25.39 (± 28.84) | | | |
| Week 36 (n=230) | -28.13 (± 29.01) | | | |
| Week 48 (n=223) | -24.72 (± 29.38) | | | |
| Week 60 (n=222) | -26.44 (± 28.03) | | | |
| Week 72 (n=200) | -25.06 (± 29.84) | | | |
| Week 84 (n=193) | -23.62 (± 29.25) | | | |
| Week 96 (n=193) | -27.06 (± 30.60) | | | |
| Week 120 (n=172) | -24.15 (± 31.14) | | | |
| Week 144 (n=168) | -23.97 (± 32.05) | | | |
| Week 168 (n=162) | -24.59 (± 31.16) | | | |
| Week 192 (n=155) | -24.77 (± 29.63) | | | |
| Week 216 (n=136) | -24.54 (± 31.55) | | | |
| Week 240 (n=140) | -25.05 (± 29.26) | | | |
| Week 264 (n=122) | -27.10 (± 28.75) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Work Productivity and Activity Impairment: Percent Activity Impairment due to RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, and ACT11575 only

| | |
|-----------------|---|
| End point title | Change From Baseline in Work Productivity and Activity Impairment: Percent Activity Impairment due to RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210 - Subjects From EFC11072, and ACT11575 only |
|-----------------|---|

End point description:

WPAI assesses work productivity and impairment. It is 6-item questionnaire to assess degree to which RA affected work productivity & regular activities over past 7 days. Questions: Q1=current employment; Q2=hrs missed due to RA; Q3=hrs missed due to other reasons; Q4=hrs actually worked; Q5=RA affected productivity while working (0 to 10 scale, with higher numbers indicated less productivity); Q6 = RA affected regular activities (0-10 scale, with higher numbers=greater impairment). Percent activity impairment due to RA was a subscale and calculated as: $10 \times Q6$ for all respondents. Subscale score=expressed as impairment percentage (range: 0-100%) where higher numbers indicate greater impairment. Here, Baseline: Baseline of initial studies (EFC11072 and ACT11575). Safety population. Here, 'number of subjects analysed'=subjects from studies EFC11072, and ACT11575 evaluable for this endpoint and 'n'=subjects with data. Data was not planned to be collected for Sarilumab Monotherapy arm.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC11072, and ACT11575 | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 1157 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=846) | -26.47 (\pm 29.30) | | | |
| Week 12 (n=1157) | -28.02 (\pm 27.44) | | | |
| Week 24 (n=1121) | -28.76 (\pm 27.62) | | | |
| Week 36 (n=1095) | -29.71 (\pm 28.03) | | | |
| Week 48 (n=1061) | -29.11 (\pm 28.28) | | | |
| Week 60 (n=1034) | -29.81 (\pm 27.78) | | | |
| Week 72 (n=1013) | -29.61 (\pm 29.02) | | | |
| Week 84 (n=985) | -30.28 (\pm 29.53) | | | |
| Week 96 (n=954) | -30.28 (\pm 28.32) | | | |
| Week 120 (n=924) | -30.42 (\pm 28.78) | | | |

| | | | | |
|--------------------|-----------------------|--|--|--|
| Week 144 (n=883) | -30.29 (\pm 28.90) | | | |
| Week 168 (n=840) | -30.64 (\pm 29.30) | | | |
| Week 192 (n=804) | -30.88 (\pm 29.36) | | | |
| Week 216 (n=753) | -30.36 (\pm 29.34) | | | |
| Week 240 0 (n=722) | -31.12 (\pm 29.63) | | | |
| Week 264 (n=645) | -31.97 (\pm 28.77) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Work Productivity Survey - Rheumatoid Arthritis (WPS-RA) at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Work Days Missed Due to Arthritis - Subjects From EFC10832 Only

| | |
|-----------------|--|
| End point title | Change From Baseline in Work Productivity Survey - Rheumatoid Arthritis (WPS-RA) at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Work Days Missed Due to Arthritis - Subjects From EFC10832 Only |
|-----------------|--|

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with arthritis over the previous month. The questionnaire was interviewer-administered and was based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Change from Baseline in number of work days missed in the last month due to arthritis by the subject was reported in the endpoint. Here, Baseline refers to the Baseline of initial study (EFC10832). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from study EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC10832 | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 145 | | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=145) | -2.72 (\pm 6.38) | | | |
| Week 12 (n=127) | -3.66 (\pm 6.80) | | | |
| Week 24 (n=125) | -3.70 (\pm 6.85) | | | |
| Week 36 (n=121) | -3.73 (\pm 7.08) | | | |

| | | | | |
|------------------|----------------|--|--|--|
| Week 48 (n=116) | -3.37 (± 7.18) | | | |
| Week 60 (n=114) | -3.55 (± 6.93) | | | |
| Week 72 (n=111) | -3.58 (± 7.07) | | | |
| Week 84 (n=106) | -3.11 (± 8.49) | | | |
| Week 96 (n=101) | -3.47 (± 7.57) | | | |
| Week 120 (n=101) | -3.54 (± 7.56) | | | |
| Week 144 (n=94) | -3.51 (± 6.84) | | | |
| Week 168 (n=88) | -3.73 (± 7.37) | | | |
| Week 192 (n=80) | -3.76 (± 7.21) | | | |
| Week 216 (n=74) | -3.51 (± 7.30) | | | |
| Week 240 (n=73) | -2.44 (± 6.70) | | | |
| Week 264 (n=66) | -2.86 (± 5.83) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Days With Work Productivity Reduced by $\geq 50\%$ Due to Arthritis - Subjects From EFC10832 Only

| | |
|-----------------|--|
| End point title | Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Days With Work Productivity Reduced by $\geq 50\%$ Due to Arthritis - Subjects From EFC10832 Only |
|-----------------|--|

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire was interviewer-administered and was based on subjects self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Change from Baseline in number of work days with work productivity reduced by $\geq 50\%$ by the subjects was reported in the endpoint. Here, Baseline refers to the Baseline of initial study (EFC10832). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from study EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC10832 | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 145 | | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=145) | -3.47 (± 7.64) | | | |
| Week 12 (n=126) | -4.93 (± 9.22) | | | |
| Week 24 (n=123) | -5.14 (± 7.67) | | | |
| Week 36 (n=122) | -5.47 (± 8.41) | | | |

| | | | | |
|------------------|----------------|--|--|--|
| Week 48 (n=115) | -5.75 (± 8.14) | | | |
| Week 60 (n=114) | -5.16 (± 7.96) | | | |
| Week 72 (n=110) | -5.21 (± 7.74) | | | |
| Week 84 (n=105) | -4.40 (± 8.27) | | | |
| Week 96 (n=101) | -5.03 (± 6.91) | | | |
| Week 120 (n=101) | -4.63 (± 7.47) | | | |
| Week 144 (n=94) | -4.88 (± 7.53) | | | |
| Week 168 (n=88) | -4.67 (± 7.06) | | | |
| Week 192 (n=80) | -4.55 (± 7.25) | | | |
| Week 216 (n=74) | -4.42 (± 8.01) | | | |
| Week 240 (n=73) | -3.48 (± 7.56) | | | |
| Week 264 (n=66) | -3.97 (± 5.02) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Arthritis Interference With Work Productivity - Subjects From EFC10832 Only

| | |
|-----------------|--|
| End point title | Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Arthritis Interference With Work Productivity - Subjects From EFC10832 Only |
|-----------------|--|

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire was interviewer-administered and was based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Interference in the last month with work productivity was measured on a scale that ranges from 0 (no interference) to 10 (complete interference), where higher scores indicated more interference. Here, Baseline refers to the Baseline of initial study (EFC10832). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from study EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC10832 | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 144 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=144) | -20.83 (± 30.51) | | | |
| Week 12 (n=127) | -27.95 (± 58.67) | | | |

| | | | | |
|-------------------|------------------|--|--|--|
| Week 24 (n=124) | -35.16 (± 31.45) | | | |
| Week 36 (n=123) | -37.48 (± 33.72) | | | |
| Week 48 (n=115) | -36.78 (± 31.58) | | | |
| Week 60 (n=115) | -40.35 (± 33.19) | | | |
| Week 72 (n=111) | -38.74 (± 32.73) | | | |
| Week 84 (n=106) | -39.62 (± 41.56) | | | |
| Week 96 (n=102) | -42.35 (± 32.19) | | | |
| Week 120 (n=102) | -37.84 (± 32.32) | | | |
| Week 144 (n=95) | -39.16 (± 32.28) | | | |
| Week 168 (n=90) | -38.11 (± 32.25) | | | |
| Week 192 (n=81) | -40.74 (± 34.96) | | | |
| Week 216 (n=74) | -39.19 (± 37.00) | | | |
| Week 240 0 (n=73) | -38.22 (± 38.24) | | | |
| Week 264 (n=66) | -39.24 (± 36.09) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: House Work Days Missed due to Arthritis - Subjects From EFC10832 Only

| | |
|-----------------|--|
| End point title | Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: House Work Days Missed due to Arthritis - Subjects From EFC10832 Only |
|-----------------|--|

End point description:

'The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire was interviewer-administered and was based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Change from baseline in number of days with no household work//household work missed in the last month by the subjects was reported. Here, Baseline refers to the Baseline of initial study (EFC10832). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from study EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC10832 | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 446 | | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=446) | -4.65 (± 9.44) | | | |
| Week 12 (n=401) | -6.17 (± 10.29) | | | |
| Week 24 4 (n=397) | -6.55 (± 9.92) | | | |
| Week 36 (n=388) | -6.65 (± 10.36) | | | |
| Week 48 (n=373) | -6.61 (± 10.57) | | | |
| Week 60 (n=364) | -6.84 (± 10.47) | | | |
| Week 72 (n=355) | -6.50 (± 10.72) | | | |
| Week 84 (n=343) | -6.56 (± 10.63) | | | |
| Week 96 (n=336) | -6.80 (± 10.32) | | | |
| Week 120 (n=323) | -6.81 (± 10.31) | | | |
| Week 144 (n=309) | -6.78 (± 10.67) | | | |
| Week 168 (n=283) | -7.04 (± 10.13) | | | |
| Week 192 (n=274) | -6.74 (± 10.51) | | | |
| Week 216 (n=261) | -6.78 (± 10.07) | | | |
| Week 240 (n=243) | -6.82 (± 10.02) | | | |
| Week 264 (n=230) | -6.95 (± 10.16) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Days With Household Work Productivity Reduced by >=50% Due to Arthritis - Subjects From EFC10832 Only

| | |
|-----------------|--|
| End point title | Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Days With Household Work Productivity Reduced by >=50% Due to Arthritis - Subjects From EFC10832 Only |
|-----------------|--|

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire was interviewer-administered and

was based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Change from baseline in number of days with reduced household work productivity by $\geq 50\%$ in the last month by the subjects was reported. Here, Baseline refers to the Baseline of initial study (EFC10832). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from study EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC10832 | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 445 | | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=445) | -4.08 (\pm 10.24) | | | |
| Week 12 (n=402) | -5.64 (\pm 10.93) | | | |
| Week 24 (n=395) | -6.01 (\pm 10.40) | | | |
| Week 36 (n=387) | -6.57 (\pm 10.29) | | | |
| Week 48 (n=372) | -7.06 (\pm 10.13) | | | |
| Week 60 (n=363) | -7.01 (\pm 10.30) | | | |
| Week 72 (n=353) | -6.70 (\pm 10.72) | | | |
| Week 84 (n=342) | -6.38 (\pm 10.79) | | | |
| Week 96 (n=334) | -7.05 (\pm 10.62) | | | |
| Week 120 (n=322) | -7.12 (\pm 10.37) | | | |
| Week 144 (n=308) | -6.58 (\pm 10.59) | | | |
| Week 168 (n=284) | -6.39 (\pm 10.28) | | | |
| Week 192 (n=274) | -6.01 (\pm 10.07) | | | |
| Week 216 (n=259) | -6.27 (\pm 10.30) | | | |
| Week 240 (n=241) | -6.31 (\pm 9.99) | | | |
| Week 264 (n=229) | -6.93 (\pm 9.43) | | | |

Statistical analyses

Secondary: Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Days With Family/Social/Leisure Activities Missed Due to Arthritis - Subjects From EFC10832 Only

| | |
|-----------------|---|
| End point title | Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Days With Family/Social/Leisure Activities Missed Due to Arthritis - Subjects From EFC10832 Only |
|-----------------|---|

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire was interviewer-administered and was based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Change from baseline in number of days missed of family/social/leisure activities in the last month by the subjects was reported. Here, Baseline refers to the Baseline of initial study (EFC10832). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from study EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC10832 | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 447 | | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=447) | -2.94 (± 8.34) | | | |
| Week 12 (n=401) | -4.16 (± 8.38) | | | |
| Week 24 (n=397) | -4.50 (± 8.42) | | | |
| Week 36 (n=388) | -4.38 (± 8.88) | | | |
| Week 48 (n=373) | -4.44 (± 8.51) | | | |
| Week 60 (n=364) | -4.46 (± 8.31) | | | |
| Week 72 (n=354) | -4.20 (± 8.52) | | | |
| Week 84 (n=343) | -4.31 (± 8.30) | | | |
| Week 96 (n=335) | -4.38 (± 8.03) | | | |
| Week 120 (n=323) | -4.43 (± 8.01) | | | |
| Week 144 (n=309) | -4.17 (± 7.90) | | | |
| Week 168 (n=285) | -4.12 (± 8.16) | | | |
| Week 192 (n=272) | -4.23 (± 8.17) | | | |
| Week 216 (n=261) | -3.93 (± 8.03) | | | |
| Week 240 (n=242) | -4.03 (± 8.26) | | | |
| Week 264 (n=230) | -3.85 (± 7.65) | | | |

Statistical analyses

Secondary: Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Days With Outside Help Hired Due to Arthritis- Subjects From EFC10832 Only

| | |
|-----------------|---|
| End point title | Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Days With Outside Help Hired Due to Arthritis- Subjects From EFC10832 Only |
|-----------------|---|

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire was interviewer-administered and was based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). Change from baseline in number of days with outside help hired in the last month by the subject was reported. Here, Baseline refers to the Baseline of initial study (EFC10832). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from study EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in protocol.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC10832 | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 446 | | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=446) | -2.92 (± 10.14) | | | |
| Week 12 (n=401) | -4.24 (± 10.16) | | | |
| Week 24 (n=397) | -4.12 (± 10.47) | | | |
| Week 36 (n=388) | -4.28 (± 10.27) | | | |
| Week 48 (n=373) | -4.58 (± 10.12) | | | |
| Week 60 (n=364) | -4.21 (± 10.16) | | | |
| Week 72 (n=354) | -4.00 (± 9.52) | | | |
| Week 84 (n=343) | -3.81 (± 9.67) | | | |
| Week 96 (n=335) | -3.90 (± 10.11) | | | |
| Week 120 (n=323) | -3.90 (± 9.62) | | | |
| Week 144 (n=309) | -3.91 (± 9.73) | | | |
| Week 168 (n=285) | -4.14 (± 10.00) | | | |
| Week 192 (n=273) | -3.93 (± 10.14) | | | |
| Week 216 (n=261) | -4.19 (± 9.84) | | | |
| Week 240 (n=242) | -4.12 (± 10.43) | | | |

| | | | | |
|------------------|----------------|--|--|--|
| Week 264 (n=230) | -4.05 (± 9.67) | | | |
|------------------|----------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Arthritis Interference With Household Work Productivity - Subjects From EFC10832 Only

| | |
|-----------------|--|
| End point title | Change From Baseline in WPS-RA at Weeks 0, 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210: Arthritis Interference With Household Work Productivity - Subjects From EFC10832 Only |
|-----------------|--|

End point description:

The WPS-RA is a validated questionnaire that evaluates productivity limitations within work and within home associated with RA over the previous month. The questionnaire was interviewer-administered and was based on subject self-report. It contains 9 questions addressing employment status (1 item), productivity at work (3 items), and within and outside the home (5 items). The RA interference in the last month with household work productivity was measured on a scale that ranged from 0 (no interference) to 10 (complete interference), where higher scores indicated more interference. Here, Baseline refers to the Baseline of initial study (EFC10832). Analysis was performed on safety population. Here, 'number of subjects analysed' = subjects from study EFC10832 evaluable for this endpoint and 'n' = subjects with available data for each specified category. Data for this endpoint was not planned to be collected and analysed for Sarilumab Monotherapy arm, as pre-specified in the protocol.

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

End point timeframe:

Baseline, Weeks 0 (post-dose), 12, 24, 36, 48, 60, 72, 84, 96, 120, 144, 168, 192, 216, 240 and 264 of LTS11210

| End point values | Sarilumab + DMARD: EFC10832 | | | |
|--------------------------------------|-----------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 444 | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 0 (n=444) | -23.24 (± 35.09) | | | |
| Week 12 (n=401) | -33.49 (± 35.76) | | | |
| Week 24 (n=399) | -36.94 (± 36.75) | | | |
| Week 36 (n=388) | -36.42 (± 39.35) | | | |
| Week 48 (n=373) | -37.45 (± 34.85) | | | |
| Week 60 (n=365) | -38.19 (± 34.55) | | | |
| Week 72 (n=355) | -36.48 (± 35.37) | | | |

| | | | | |
|------------------|------------------|--|--|--|
| Week 84 (n=344) | -35.61 (± 39.69) | | | |
| Week 96 (n=335) | -36.81 (± 36.04) | | | |
| Week 120 (n=324) | -38.86 (± 35.22) | | | |
| Week 144 (n=310) | -36.23 (± 37.52) | | | |
| Week 168 (n=286) | -36.01 (± 39.84) | | | |
| Week 192 (n=274) | -35.80 (± 40.99) | | | |
| Week 216 (n=260) | -38.54 (± 39.81) | | | |
| Week 240 (n=240) | -40.08 (± 35.68) | | | |
| Week 264 (n=228) | -38.07 (± 42.39) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Sub-study: Number of subjects who Reported Adverse Events Related to Pre-filled Syringe With Safety System

| | |
|-----------------|--|
| End point title | Sub-study: Number of subjects who Reported Adverse Events Related to Pre-filled Syringe With Safety System |
|-----------------|--|

End point description:

AEs related to PFS-S included PTC-related AEs, device-related AEs, or AEs of injection site reaction. In this endpoint, only PTC-related AEs, device-related AEs, or AEs of injection site reaction assessed during the sub-study were reported. TEAEs and SAEs reported during the sub-study were included in the main study data and no separate data collection and analysis was performed, as pre-planned in the protocol. Analysis was performed on all subjects who were enrolled in the sub-study.

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

End point timeframe:

From Week 24 to 36

| End point values | PFS-S Sarilumab 150 mg q2w | PFS-S Sarilumab 200 mg q2w | PFS-S Sarilumab 200 to 150 mg q2w | |
|--------------------------------|----------------------------------|----------------------------------|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 25 | 98 | 1 | |
| Units: subejcts | | | | |
| PTC-related AEs | 0 | 0 | 0 | |
| Device-related AEs | 0 | 0 | 0 | |
| AEs of injection site reaction | 0 | 0 | 0 | |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose (i.e., Day 1 of study LTS11210) of IMP to last dose of IMP + 60 days (maximum duration: up to 523 weeks)

Adverse event reporting additional description:

Reported AEs and deaths were TEAEs that developed/worsened in grade or became serious during TEAE period (defined as time from 1st dose of IMP to last dose of IMP + 60 days). As pre-specified and initially planned, TEAEs and SAEs reported during sub-study were included in the main study data and no separate analysis was done. Safety population.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) |
|-----------------------|--|

Reporting group description:

Subjects who completed any of initial studies: Part A or B of EFC11072, ACT11575, EFC10832 or SFY13370 were enrolled in LTS11210 and received sarilumab 150 milligrams (mg) subcutaneously (SC) once weekly (qw). Dose could be reduced to 150 mg every 2 weeks (q2w) due to neutropenia, thrombocytopenia or increase in liver enzymes (alanine aminotransferase [ALT]). After dose regimens selection for Phase 3 studies (150 mg q2w and 200 mg q2w), subjects already receiving 150 mg qw were switched to sarilumab 200 mg q2w. Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks). Subjects who were already taking concomitant non-biologic DMARDs in initial study continued stable dose of one or combination of conventional synthetic DMARDs they were taking.

| | |
|-----------------------|-----------------------|
| Reporting group title | Sarilumab monotherapy |
|-----------------------|-----------------------|

Reporting group description:

Subjects who completed study EFC13752 were enrolled in LTS11210 and received sarilumab 200 mg q2w. Dose could be reduced to 150 mg q2w due to neutropenia, thrombocytopenia or increase in liver enzymes (ALT). Treatment duration per subject was at least 264 weeks from first study drug administration in LTS11210. Subjects continued to be treated beyond 264 weeks until sarilumab was commercially available in their respective countries or until 2020, at the latest (maximum duration: 523 weeks).

| Serious adverse events | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | |
|---|--|-----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 617 / 1910 (32.30%) | 27 / 111 (24.32%) | |
| number of deaths (all causes) | 49 | 3 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma Of Colon | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ameloblastoma | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Squamous Cell Carcinoma | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| B-Cell Lymphoma | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal Cell Carcinoma | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 6 / 1910 (0.31%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign Neoplasm Of Thyroid Gland | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder Cancer Stage Ii | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | | |
|--|------------------------------------|-----------------------------------|--|--|
| Breast Cancer alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 1 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Breast Cancer Stage Ii alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Bronchial Carcinoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Cervix Cancer Metastatic alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 1 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Cholesteatoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Clear Cell Renal Cell Carcinoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Colorectal Adenocarcinoma alternative dictionary used: MedDRA 23.1 | | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal Cancer Metastatic alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Eye Naevus alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibroadenoma Of Breast alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibroma alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder Cancer Metastatic alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Invasive Ductal Breast Carcinoma alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | | |
|---|------------------|-----------------|--|--|
| Lung Adenocarcinoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| Lung Cancer Metastatic alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Lung Carcinoma Cell Type Unspecified Stage Iii alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Lung Neoplasm Malignant alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Malignant Melanoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Metastatic Renal Cell Carcinoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Neoplasm Malignant alternative dictionary used: MedDRA 23.1 | | | | |

| | | | |
|--|------------------|-----------------|--|
| subjects affected / exposed | 0 / 1910 (0.00%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Non-Small Cell Lung Cancer alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Ovarian Cancer alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian Germ Cell Teratoma Benign alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary Thyroid Cancer alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parathyroid Tumour Benign alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pituitary Tumour Benign alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------------------------|-----------------------------------|--|--|
| Pleomorphic Adenoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Prostate Cancer alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Prostatic Adenoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 1 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Rectal Cancer alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Refractory Anaemia With An Excess Of Blasts alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Renal Cell Carcinoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Serous Cystadenocarcinoma Ovary alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin Cancer | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small Intestine Carcinoma | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous Cell Carcinoma Of Skin | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous Cell Carcinoma Of The Cervix | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine Leiomyoma | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 7 / 1910 (0.37%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Accelerated Hypertension | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic Embolus | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriosclerosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep Vein Thrombosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 8 / 1910 (0.42%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive Crisis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|------------------------------------|-----------------------------------|--|--|
| Hypotension alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Hypovolaemic Shock alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Iliac Artery Embolism alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pelvic Venous Thrombosis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Peripheral Artery Occlusion alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Peripheral Embolism alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Peripheral Ischaemia alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral Venous Disease alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicose Vein alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous Thrombosis Limb alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Missed alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abortion Spontaneous alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 4 / 1910 (0.21%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy alternative dictionary used: MedDRA 23.1 | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 0 / 1910 (0.00%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Cardiac Death | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Chills | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Multiple Organ Dysfunction Syndrome | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 0 | |
| Non-Cardiac Chest Pain | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 6 / 1910 (0.31%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden Death | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Social circumstances | | | |
| Pregnancy Of Partner | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Acquired Hydrocele | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adnexa Uteri Cyst | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign Prostatic Hyperplasia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast Enlargement | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast Hyperplasia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical Dysplasia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical Polyp alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial Hyperplasia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometriosis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Menometrorrhagia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|------------------------------------|-----------------------------------|--|
| Menorrhagia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Ovarian Cyst alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 1910 (0.21%) 0 / 4 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Pelvic Prolapse alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Uterine Haemorrhage alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | |
| Uterine Prolapse alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Vaginal Haemorrhage alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders Acute Pulmonary Oedema alternative dictionary used: MedDRA 23.1 | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Acute Respiratory Failure alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Asthma alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atelectasis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial Hyperreactivity alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic Obstructive Pulmonary Disease alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diaphragmatic Abnormal Relaxation alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Emphysema | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Epistaxis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Idiopathic Pulmonary Fibrosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial Lung Disease | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Infiltration | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------------------------|-----------------------------------|--|--|
| Pleural Effusion alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 1910 (0.21%) 0 / 4 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pleurisy alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 1 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pneumonia Aspiration alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pneumonitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pneumothorax alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 2 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pneumothorax Spontaneous alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 1 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pulmonary Embolism alternative dictionary used: MedDRA 23.1 | | | | |

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|---|-------------------|-----------------|--|
| subjects affected / exposed | 10 / 1910 (0.52%) | 2 / 111 (1.80%) | |
| occurrences causally related to treatment / all | 1 / 10 | 0 / 3 | |
| deaths causally related to treatment / all | 1 / 2 | 0 / 0 | |
| Pulmonary Fibrosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Hypertension | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Mass | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory Failure | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sleep Apnoea Syndrome | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Acute Psychosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcohol Abuse | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bipolar Disorder | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Conversion Disorder | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major Depression | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mixed Anxiety And Depressive Disorder | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paranoia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal Ideation | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide Attempt | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device Breakage | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device Dislocation | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device Loosening | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device Malfunction | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine Aminotransferase Increased alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 9 / 1910 (0.47%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 7 / 9 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fungal Test Positive alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiv Test False Positive alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil Count Decreased alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oxygen Saturation Decreased alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transaminases Increased alternative dictionary used: MedDRA 23.1 | | | |

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| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Abdominal Injury | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental Overdose | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcohol Poisoning | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Anaemia Postoperative | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle Fracture | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bite | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Comminuted Fracture alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Craniocerebral Injury alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dislocation Of Vertebra alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral Neck Fracture alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 8 / 1910 (0.42%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur Fracture alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 7 / 1910 (0.37%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|------------------------------------|-----------------------------------|--|--|
| Foot Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Fractured Sacrum alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Gastrointestinal Stoma Complication alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Gun Shot Wound alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Hip Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 5 / 1910 (0.26%) 0 / 5 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Humerus Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 5 / 1910 (0.26%) 0 / 5 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | | |
| Incision Site Fibrosis alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incisional Hernia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint Dislocation alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament Sprain alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower Limb Fracture alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple Injuries alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Patella Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pelvic Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Periorbital Haematoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Periprosthetic Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Periprosthetic Osteolysis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Post Procedural Fistula alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Post Procedural Haematoma alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post Procedural Haemorrhage alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural Pain alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural Shock alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius Fracture alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal Compression Fracture alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 5 / 1910 (0.26%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal Fracture alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Subdural Haematoma alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Tendon Rupture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 5 / 1910 (0.26%) 0 / 5 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Thermal Burn alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Tibia Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 5 / 1910 (0.26%) 0 / 5 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Toxicity To Various Agents alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Ulna Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 1910 (0.21%) 0 / 4 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Cardiac disorders Acute Coronary Syndrome alternative dictionary used: MedDRA 23.1 | | | |

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|---|-------------------|-----------------|--|
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute Left Ventricular Failure alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Acute Myocardial Infarction alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 11 / 1910 (0.58%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 11 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina Pectoris alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina Unstable alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial Fibrillation alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 9 / 1910 (0.47%) | 2 / 111 (1.80%) | |
| occurrences causally related to treatment / all | 2 / 11 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial Flutter alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|------------------------------------|-----------------------------------|--|--|
| Atrial Tachycardia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Atrioventricular Block Complete alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 1910 (0.00%) 0 / 0 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | | |
| Bradycardia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Cardiac Failure alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 1910 (0.21%) 0 / 4 0 / 2 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Cardiac Failure Acute alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Cardiac Failure Congestive alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 1 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Cardiac Tamponade alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardio-Respiratory Arrest alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiogenic Shock alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiomyopathy alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary Failure alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Congestive Cardiomyopathy alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary Artery Disease alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|------------------|-----------------|--|--|
| Coronary Artery Perforation alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Coronary Artery Stenosis alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Left Ventricular Failure alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 1 / 111 (0.90%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | | |
| Microvascular Coronary Artery Disease alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Myocardial Infarction alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 5 / 1910 (0.26%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| Myocardial Ischaemia alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 4 / 1910 (0.21%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Pericarditis alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus Node Dysfunction alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular Tachycardia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular Asystole alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular Fibrillation alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Amnesia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carpal Tunnel Syndrome alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 4 / 1910 (0.21%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebellar Stroke | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral Haematoma | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral Infarction | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular Accident | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 5 / 1910 (0.26%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cerebrovascular Insufficiency | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depressed Level Of Consciousness | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------------------------|-----------------------------------|--|--|
| Epilepsy alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Haemorrhage Intracranial alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Haemorrhagic Stroke alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 1910 (0.00%) 0 / 0 0 / 0 | 2 / 111 (1.80%) 0 / 2 0 / 0 | | |
| Haemorrhagic Transformation Stroke alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Intraventricular Haemorrhage alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Ischaemic Stroke alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | | |
| Lumbar Radiculopathy alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multifocal Motor Neuropathy | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelopathy | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Partial Seizures | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral Sensory Neuropathy | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiculopathy | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Ruptured Cerebral Aneurysm alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| Sciatica alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Seizure alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Subarachnoid Haemorrhage alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | | |
| deaths causally related to treatment / all | 1 / 2 | 0 / 0 | | |
| Syncope alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 4 / 1910 (0.21%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Transient Global Amnesia alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Transient Ischaemic Attack alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 6 / 1910 (0.31%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular Headache | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Anaemia Megaloblastic | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood Loss Anaemia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone Marrow Failure | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile Neutropenia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|-------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iron Deficiency Anaemia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 0 / 1910 (0.00%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphatic Insufficiency | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 11 / 1910 (0.58%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 12 / 12 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 4 / 1910 (0.21%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spontaneous Haemorrhage | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Thrombocytopenia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 1 / 3 0 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Eye disorders | | | |
| Cataract alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 1910 (0.21%) 0 / 4 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Central Vision Loss alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Choroiditis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Dry Age-Related Macular Degeneration alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Macular Hole alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Neovascular Age-Related Macular Degeneration alternative dictionary used: | | | |

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| MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Optic Ischaemic Neuropathy | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal Vascular Thrombosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicolith | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic Gastritis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 0 / 1910 (0.00%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crohn's Disease | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticular Perforation alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum Intestinal alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum Intestinal Haemorrhagic alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal Perforation alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterovesical Fistula alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral Hernia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------------------------|-----------------------------------|--|--|
| Gastric Haemorrhage alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 1910 (0.00%) 0 / 0 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | | |
| Gastric Ulcer Perforation alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Gastritis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Gastrointestinal Inflammation alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Gastrooesophageal Reflux Disease alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Haemorrhoidal Haemorrhage alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Haemorrhoids alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hernial Eventration | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus Hernia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileal Perforation | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 0 / 1910 (0.00%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated Umbilical Hernia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inflammatory Bowel Disease | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|------------------------------------|-----------------------------------|--|--|
| Inguinal Hernia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Intestinal Dilatation alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Intestinal Obstruction alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Irritable Bowel Syndrome alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Large Intestine Perforation alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 1 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Noninfectious Peritonitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pancreatic Necrosis alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic Pseudocyst Haemorrhage alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis Acute alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 5 / 1910 (0.26%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis Necrotising alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 0 / 1910 (0.00%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritoneal Adhesions alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal Haemorrhage alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------------------------|-----------------------------------|--|
| Small Intestinal Obstruction alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 5 0 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Rectal Prolapse alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Umbilical Hernia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Upper Gastrointestinal Haemorrhage alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Hepatobiliary disorders Bile Duct Stone alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 3 / 1910 (0.16%) 0 / 3 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | |
| Cholecystitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 9 / 1910 (0.47%) 0 / 9 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Cholecystitis Acute alternative dictionary used: MedDRA 23.1 | | | |

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|---|-------------------|-----------------|--|
| subjects affected / exposed | 3 / 1910 (0.16%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 24 / 1910 (1.26%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 24 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis Chronic | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis Obstructive | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Portosplenomesenteric Venous Thrombosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Cutaneous Lupus Erythematosus | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decubitus Ulcer | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatomyositis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erythema Multiforme | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 0 / 1910 (0.00%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin Necrosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin Ulcer | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous Emphysema | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxic Skin Eruption | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Renal and urinary disorders | | | |
| Acute Kidney Injury | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus Urinary | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 0 / 1910 (0.00%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis Haemorrhagic | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hydronephrosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 7 / 1910 (0.37%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal Colic | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureterolithiasis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral Stenosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Incontinence | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Goitre | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroiditis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroiditis Subacute | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Ankle Deformity | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 6 / 1910 (0.31%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atlantoaxial Subluxation | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back Pain | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone Cyst | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|--------------------------------------|-----------------------------------|--|--|
| Costochondritis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Fasciitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Flank Pain alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Foot Deformity alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 14 / 1910 (0.73%) 0 / 19 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Hand Deformity alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Intervertebral Disc Degeneration alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | | |
| Intervertebral Disc Disorder alternative dictionary used: MedDRA 23.1 | | | | |

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|---|-------------------|-----------------|--|
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral Disc Protrusion alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint Destruction alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Knee Deformity alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar Spinal Stenosis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 45 / 1910 (2.36%) | 2 / 111 (1.80%) | |
| occurrences causally related to treatment / all | 0 / 52 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|--------------------------------------|-----------------------------------|--|--|
| Osteoporotic Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pathological Fracture alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Rheumatoid Arthritis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 32 / 1910 (1.68%) 3 / 33 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | | |
| Rheumatoid Nodule alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Rotator Cuff Syndrome alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Spinal Osteoarthritis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Spinal Stenosis alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 4 / 1910 (0.21%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondylolisthesis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovitis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist Deformity | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal Abscess | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess Limb | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 6 / 1910 (0.31%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess Neck | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess Oral | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess Soft Tissue | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute Sinusitis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal Abscess | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 4 / 1910 (0.21%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriovenous Graft Site Infection | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------------------------|-----------------------------------|--|--|
| Arthritis Bacterial alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 6 / 1910 (0.31%) 5 / 7 0 / 0 | 1 / 111 (0.90%) 1 / 1 0 / 0 | | |
| Arthritis Infective alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Atypical Pneumonia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Bacteraemia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Bacterial Dacryocystitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Bartholin's Abscess alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Bone Tuberculosis alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 4 / 1910 (0.21%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis Fungal | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bullous Erysipelas | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis Infective | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Covid-19 Pneumonia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carbuncle | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|-------------------|-----------------|--|--|
| Cellulitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 21 / 1910 (1.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 15 / 24 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Cellulitis Staphylococcal alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Cholecystitis Infective alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Clostridium Difficile Infection alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 2 / 111 (1.80%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| Coccidioidomycosis alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Colonic Abscess alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Dengue Fever alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device Related Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea Infectious alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 7 / 1910 (0.37%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 2 / 7 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocarditis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometritis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis Infectious alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|------------------------------------|-----------------------------------|--|--|
| Epiglottitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 1910 (0.00%) 0 / 0 0 / 0 | 1 / 111 (0.90%) 0 / 1 0 / 0 | | |
| Erysipelas alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 5 / 1910 (0.26%) 3 / 5 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Escherichia Urinary Tract Infection alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Extradural Abscess alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Gangrene alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Gas Gangrene alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Gastroenteritis alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis Bacterial alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis Salmonella alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis Viral alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes Ophthalmic alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes Zoster alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 5 / 1910 (0.26%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 5 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------|-----------------|--|--|
| Histoplasmosis Disseminated alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| Infected Bite alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Infected Skin Ulcer alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 6 / 1910 (0.31%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 5 / 6 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Infectious Pleural Effusion alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| Infective Exacerbation Of Bronchiectasis alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Infective Exacerbation Of Chronic Obstructive Airways Disease alternative dictionary used: MedDRA 23.1 | | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Large Intestine Infection alternative dictionary used: MedDRA 23.1 | | | | |

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|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leptospirosis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver Abscess | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised Infection | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Abscess | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lyme Disease | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Medical Device Site Joint Infection | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------|-----------------|--|--|
| Meningitis Viral alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Meningoencephalitis Herpetic alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Muscle Abscess alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Necrotising Fasciitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Necrotising Soft Tissue Infection alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Ophthalmic Herpes Zoster alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Oral Candidiasis alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 6 / 1910 (0.31%) | 1 / 111 (0.90%) | |
| occurrences causally related to treatment / all | 3 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis Acute alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreas Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic Abscess alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perineal Abscess alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 7 / 1910 (0.37%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--|---------------------------------------|-----------------------------------|--|--|
| Pneumonia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 52 / 1910 (2.72%) 25 / 55 1 / 5 | 1 / 111 (0.90%) 0 / 1 0 / 0 | | |
| Pneumonia Chlamydial alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pneumonia Pneumococcal alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pneumonia Streptococcal alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 1910 (0.10%) 0 / 2 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Pneumonia Viral alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 1 / 1 1 / 1 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Post Procedural Infection alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | | |
| Postoperative Abscess alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative Wound Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psoas Abscess alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Pulmonary Tuberculosis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis Acute alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 5 / 1910 (0.26%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 4 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis Chronic alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------|-----------------|--|--|
| Relapsing Fever alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Renal Abscess alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Respiratory Tract Infection alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Salmonellosis alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Salpingitis alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Salpingo-Oophoritis alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Sepsis alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 6 / 1910 (0.31%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 2 | 0 / 0 | |
| Septic Arthritis Neisserial alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic Shock alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 6 / 1910 (0.31%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 3 | 0 / 0 | |
| Sialoadenitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft Tissue Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal Bacteraemia alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------|-----------------|--|--|
| Staphylococcal Infection alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Staphylococcal Skin Infection alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Subcutaneous Abscess alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 5 / 1910 (0.26%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Subdural Abscess alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Tooth Abscess alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Tuberculosis alternative dictionary used: MedDRA 23.1 subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Tubo-Ovarian Abscess alternative dictionary used: MedDRA 23.1 | | | | |

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|--|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper Respiratory Tract Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Tract Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 4 / 1910 (0.21%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral Myositis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound Infection Staphylococcal alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|------------------------------------|-----------------------------------|--|
| Wound Sepsis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Metabolism and nutrition disorders Dehydration alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Diabetes Mellitus alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Diabetes Mellitus Inadequate Control alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Diabetic Ketoacidosis alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Hyperglycaemia alternative dictionary used: MedDRA 23.1 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 1910 (0.05%) 0 / 1 0 / 0 | 0 / 111 (0.00%) 0 / 0 0 / 0 | |
| Hyperglycaemic Hyperosmolar Nonketotic Syndrome alternative dictionary used: MedDRA 23.1 | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertriglyceridaemia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 2 / 1910 (0.10%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Latent Autoimmune Diabetes In Adults | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obesity | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

| | | | |
|---|------------------|-----------------|--|
| subjects affected / exposed | 3 / 1910 (0.16%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour Lysis Syndrome | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 1 / 1910 (0.05%) | 0 / 111 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Sarilumab + Disease Modifying Anti-Rheumatic Drugs (DMARD) | Sarilumab monotherapy | |
|---|--|-----------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1444 / 1910 (75.60%) | 82 / 111 (73.87%) | |
| Investigations | | | |
| Alanine Aminotransferase Increased | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 201 / 1910 (10.52%) | 4 / 111 (3.60%) | |
| occurrences (all) | 287 | 4 | |
| Injury, poisoning and procedural complications | | | |
| Accidental Overdose | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 330 / 1910 (17.28%) | 20 / 111 (18.02%) | |
| occurrences (all) | 496 | 22 | |
| Fall | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 109 / 1910 (5.71%) | 3 / 111 (2.70%) | |
| occurrences (all) | 122 | 3 | |
| Vascular disorders | | | |
| Hypertension | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

| | | | |
|--|------------------------|-------------------|--|
| subjects affected / exposed | 235 / 1910 (12.30%) | 4 / 111 (3.60%) | |
| occurrences (all) | 271 | 5 | |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 101 / 1910 (5.29%) | 4 / 111 (3.60%) | |
| occurrences (all) | 181 | 5 | |
| Neutropenia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 348 / 1910 (18.22%) | 18 / 111 (16.22%) | |
| occurrences (all) | 786 | 64 | |
| General disorders and administration site conditions | | | |
| Injection Site Erythema | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 111 / 1910 (5.81%) | 0 / 111 (0.00%) | |
| occurrences (all) | 751 | 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 122 / 1910 (6.39%) | 2 / 111 (1.80%) | |
| occurrences (all) | 153 | 2 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 62 / 1910 (3.25%) | 7 / 111 (6.31%) | |
| occurrences (all) | 70 | 7 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 87 / 1910 (4.55%) | 9 / 111 (8.11%) | |
| occurrences (all) | 109 | 11 | |
| Rheumatoid Arthritis | | | |
| alternative dictionary used: MedDRA 23.1 | | | |

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|--|------------------------|-------------------|--|
| subjects affected / exposed | 227 / 1910 (11.88%) | 16 / 111 (14.41%) | |
| occurrences (all) | 357 | 31 | |
| Back Pain alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 122 / 1910 (6.39%) | 6 / 111 (5.41%) | |
| occurrences (all) | 141 | 6 | |
| Infections and infestations | | | |
| Bronchitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 215 / 1910 (11.26%) | 12 / 111 (10.81%) | |
| occurrences (all) | 301 | 19 | |
| Influenza alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 124 / 1910 (6.49%) | 3 / 111 (2.70%) | |
| occurrences (all) | 160 | 4 | |
| Pharyngitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 110 / 1910 (5.76%) | 4 / 111 (3.60%) | |
| occurrences (all) | 129 | 4 | |
| Nasopharyngitis alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 249 / 1910 (13.04%) | 14 / 111 (12.61%) | |
| occurrences (all) | 390 | 26 | |
| Upper Respiratory Tract Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 303 / 1910 (15.86%) | 16 / 111 (14.41%) | |
| occurrences (all) | 574 | 21 | |
| Urinary Tract Infection alternative dictionary used: MedDRA 23.1 | | | |
| subjects affected / exposed | 264 / 1910 (13.82%) | 14 / 111 (12.61%) | |
| occurrences (all) | 428 | 22 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 10 January 2011 | <p>Following changes were performed:</p> <ul style="list-style-type: none">• Included subjects in LTS11210 study population who were randomised into and completed treatment period of ACT11575.• Indicated that study name of LTS11210 is ABILITY (Monoclonal AntiBody anti-IL-6R extensiontrial in RA for safety purposes).• Added a section that described assessment of following subject-reported outcomes health questionnaires: Functional Assessment of Chronic Illness Therapy Fatigue (FACITFatigue), Work Productivity and Activities Impairment (WPAI), Sleep Visual Analog Scale (VAS), and the SF-36 Health Survey.• Clarified that an independent joint assessor (ie, a third party who is not involved in the conduct of the study at the investigational site) was not required to carry out efficacy assessments in LTS11210 study.• Clarified hypersensitivity reactions, referred to throughout protocol as systemic hypersensitivity reactions rather than local reactions.• Specified that thrombocytopenia was an indication to decrease study drug dose regimen from 150 mg SAR153191 (subcutaneous) weekly to 150 mg SAR153191 every other week.• Indicated that prior ACT11575 subject(s) enrolled in LTS11210 study were allowed to continue use of rescue treatment, for example, sulfasalazine or leflunomide, if use was ongoing at ACT11575 end-of-treatment visit.• Deleted sIL-6Ra measurements in LTS11210 study.• Revised exclusion criterion from female of childbearing potential with a positive pregnancy test to pregnant or breastfeeding women.• Deleted exclusion criterion - Men who were unwilling to utilise 2 forms of contraception: a condom and spermicidal agent.• Indicated that absolute neutrophil count of $<500/\text{mm}^3$, lasting more than 5 days, was reported as serious adverse event.• Clarified within statistical section of LTS11210 study protocol.• Added RNA sample collection time points and modified biomarker collection time points in LTS11210 study protocol.• Provided minor clarifications to protocol. |

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|-----------------|---|
| 26 May 2011 | <ul style="list-style-type: none"> • Indicated that investigational drug product administered to subjects enrolled in LTS11210 was to be switched to new drug product, which consisted of new formulation made with different cell line, and with different drug concentrations compared to drug product that was currently in use in study. New drug product was to be packaged in prefilled syringe, compared to former drug product packaged in vial. • Clarified that after selection of Phase 3 pivotal dose(s) for program, it was intention of sponsor to switch currently enrolled subjects to highest of available selected dose regimens. All new subjects, subsequently enrolled were to be assigned to highest available selected dose regimen. Dosage switch procedure was instituted so that all enrolled subjects (preceding and proceeding pivotal dose selection) were on dose regimen with same benefit: risk ratio. • Clarified that step-down dose (due to safety issue) after selection of Phase 3 pivotal dose(s) was to be lowest available selected dose regimen. • Indicated that additional pharmaceutical form of SAR153191 (sarilumab) in amber glass vial at concentration of 100 mg/mL was to be administered to subjects enrolled into LTS11210. Use of this drug product was to be implemented, if at time of dose selection decision, selected pivotal dose regimen(s) included 200 mg dose, and/or 100 mg every other week dose. • Excluded subjects with latex hypersensitivity from enrolment because needle cap on prefilled syringe contained dry natural rubber latex particles that might cause allergic reactions. • Incorporated recently assigned International Non-proprietary Name of sarilumab. • Provided Sponsor's guidance for medical follow-up of laboratory abnormality, by adding "Thrombocytopenia" appendix. • Removed text related to nonclinical studies of embryo-fetal development, pre-/postnatal development and fertility since final study results were now formally presented in updated Investigator's Brochure. • Provided minor clarifications |
| 24 January 2012 | <ul style="list-style-type: none"> • Indicated that all enrolled subjects in LTS11210 were to be assigned to highest available sarilumab dose, 200 mg q2w dose and step-down dose (in case of specified safety issue) was to be 150 mg q2w. 150 mg and 200 mg q2w doses were selected based on analysis of completed and locked Part A study results. • Included subjects in LTS11210 population who were randomised into and completed treatment period of EFC10832. • Removed 7-day screening period from design and flowchart for subjects rolling over into LTS11210 that were previously randomised into EFC11072 Part B, Cohort 2 and EFC10832 and successfully completed treatment period. • Revised study name from ABILITY to SARIL-RA-EXTEND. • Added Week 10 visit blood samples for hematology and liver function tests (LFTs) to insure collection of hematology and LFTs every 2 weeks for initial 12 weeks of LTS11210, which mirrors schedule in EFC11072. • Provided summary of EFC11072, Part A results. • Indicated that Cardiovascular Adjudication Committee was to be established for LTS11210 to ensure that cardiovascular events were evaluated with consistent criteria and in unbiased manner. • Modified Exclusion criterion to bring consistency between exclusion criteria applied to study populations across all preceding study protocols (EFC11072, ACT11575 and EFC10832). • Added Permitted Concomitant Treatment list that needed dose adjustment following initiation of sarilumab. • Updated description of endpoints and statistical methodology for clarification purposes. • WPS-RA was added in LTS11210 because WPS-RA was included in EFC10832. • Added Subject Safety guidelines for reporting adverse events with prespecified monitoring to be consistent with guidance provided in upcoming Phase 3 sarilumab study protocols. • Provided Investigators set of clinical criteria for diagnosing anaphylaxis and Web link to National Heart, Lung and Blood Institute for reference to clinical management of lipid disorders. • Provided minor clarifications. |

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| 08 August 2012 | <p>The following changes were made:</p> <ul style="list-style-type: none"> • Implemented new safety precautions to prevent administration of sarilumab to subjects at risk for thrombocytopenia <100 000/mm³ and/or grade 3/grade 4 neutropenia. These changes were to be implemented immediately • Provided additional safety information related to thrombocytopenia and neutropenia, and to infections. |
| 31 October 2012 | <p>The following changes were made:</p> <ul style="list-style-type: none"> • Modified to allow rollover of subjects from study SFY13370. • Modified the assessment schedule starting at 2 years from 12-week to 24-week intervals, with intervening 12-week IMP supply visits • Added yearly HIV testing starting at Week 48. • Revised scheduling of X-rays of hands and feet at EOT visit to have 14-day windows except Week 260. • Added DMARD concomitant medication restrictions. • Added FM30 latex-free formulation. • Updated IMP administration language. • Updated urine analysis language. • Updated safety language related to neurological event, anti-DNA antibodies, platelets, pregnancy and infections • Added chronic neurodegenerative disease to list of medically important events • Updated database lock language • Updated Appendix L language |
| 17 July 2014 | <ul style="list-style-type: none"> • Included subjects in LTS11210 who were randomised and completed monotherapy treatment period of EFC13752; sarilumab in LTS11210 was not administered with concomitant DMARDs in subjects of EFC13752. • Modified protocol title to remove 'on top of DMARDs' and modified other sections. • Modified Exclusion Criteria: <ul style="list-style-type: none"> - Deleted history of latex allergy (systemic hypersensitivity reaction to latex) except for subjects coming from EFC10832 or SFY13370'. - Women of childbearing potential was modified to be part of local informed consent in order to follow local guidelines - Deleted "Subjects with active or latent tuberculosis at last treatment visit in EFC11072, ACT11575, SFY13370 or EFC10832' as these subjects were to be permanently discontinued in initial studies. - Added "Subjects with temporary IMP discontinuation lasting >31 days at time of planned first dose in LTS11210 ' and "Subjects fulfilling protocol-defined criteria for permanent treatment discontinuation'. • Removed Phase 2 results and added Phase 3 results of EFC11072 Part B. • Conditions for any change in concomitant treatments including nonbiologic DMARDs, steroids, and nonsteroidal anti-inflammatory drugs and analgesics were adapted. • Modified temporary treatment discontinuation up to 3 missed doses (<=59 days). • 2 local amendments were incorporated in this global amendment. • Other minor changes: <ul style="list-style-type: none"> - Removed tuberculin skin test and serum QuantiFERON test at Week 260. - Replaced HIV yearly testing with HIV testing anytime during study when subject was at risk for this infection. - Added pharmacokinetic sampling to sampling time points for ADA beyond 2 years of study treatment to facilitate appropriate interpretation of the results. - Removed X-rays performed at Week 192 visit. - Updated total number of subjects and sites. - Improved wording throughout protocol and removed superseded text. - Modified safety section to harmonise with other ongoing sarilumab studies. - Corrected schedule inconsistencies. |

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| 31 August 2015 | <ul style="list-style-type: none"> • Sarilumab treatment in LTS11210 was extended to 264 weeks in order to allow all subjects to be treated for approximately 5 calendar years from 1st sarilumab administration. • Subjects continued to be treated beyond 264 weeks if sarilumab was not commercially available in their country at Week 264.. • In the UK, duration of treatment was 264 weeks from 1st study drug administration in LTS11210 to provide finite duration of study treatment in accordance with local requirements. • Some assessments were not performed after Week 264 as per flowcharts, including health economics assessments, 12-lead ECG, and some DAS28 components of ACR core set (after Week 264, only TJC& SJC for 28 joints, subject's global assessment of disease activity) • Week 192 X-ray was deleted in Amendment 8 and reinstated with Amendment 9. • PFS-S syringe was modified version of prefilled syringe that included needle safety shield to prevent needle stick injury. • 12-week substudy was optional and was to be conducted at limited sites in selected countries. • Prior to this amendment, the protocol required permanent discontinuation of subject from study treatment in case of opportunistic infection or possible opportunistic infection per protocol. Definition of opportunistic infection had been modified. • To ensure continuity of treatment between last administration of IMP and 1st dose of commercial sarilumab, • PK: clarified analysis of bound sarilumab concentrations. After completion of EFC11072 Part B study, decision was made to only analyse functional sarilumab concentrations. • Dealtied Serum and RNA biomarkers samples long-term storage. • Corrected 2 secondary efficacy endpoints inconsistency. • Replaced "initial study" with "LTS11210", where applicable, to clarify that treatment period of 264 weeks begins day of 1st dose of sarilumab in LTS11210. • Added active comparator to list of drugs subject might had been exposed to in prior study • Corrected minor grammatical errors. |
|----------------|--|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported