



Clinical trial results:

Open label extension study to evaluate the long-term safety and tolerability of dupilumab in patients with asthma who participated in a previous dupilumab asthma clinical study

Summary

| | |
|--------------------------|--|
| EudraCT number | 2013-003856-19 |
| Trial protocol | ES IT PL DE GB NL HU BE DK SE Outside EU/EEA |
| Global end of trial date | 11 October 2019 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 25 April 2020 |
| First version publication date | 25 April 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | LTS12551 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02134028 |
| WHO universal trial number (UTN) | U1111-1117-6745 |
| Other trial identifiers | Study Name: Liberty Asthma Traverse |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Sanofi aventis recherche & développement |
| Sponsor organisation address | 1 Avenue Pierre Brossolette, Chilly Mazarin, 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) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001501-PIP02-13 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 19 November 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 11 October 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of dupilumab in subjects with asthma who participated in a previous dupilumab asthma clinical study (DRI12544, PDY14192, EFC13579, or EFC13691).

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of adults and paediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimised. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort. Adult 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 continued the background therapy dose regimen as maintained in the parent study or as modified based on Investigator's judgment throughout the study i.e. medium or high dose of inhaled corticosteroid (ICS) and a second controller medication (eg, long-acting beta-agonist [LABA], leukotriene receptor antagonist [LTRA]) was continued throughout the study. Third controller was allowed (including daily oral corticosteroids (OCS [(prednisone or prednisolone)]) for subjects from study EFC13691). Albuterol/salbutamol or levalbuterol/levosalbutamol was given as reliever medication.

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 05 August 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Netherlands: 5 |
| Country: Number of subjects enrolled | Poland: 146 |
| Country: Number of subjects enrolled | Romania: 11 |
| Country: Number of subjects enrolled | Spain: 62 |
| Country: Number of subjects enrolled | United Kingdom: 16 |
| Country: Number of subjects enrolled | Belgium: 3 |
| Country: Number of subjects enrolled | Denmark: 3 |
| Country: Number of subjects enrolled | France: 47 |

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Germany: 44 |
| Country: Number of subjects enrolled | Hungary: 10 |
| Country: Number of subjects enrolled | Italy: 36 |
| Country: Number of subjects enrolled | Japan: 160 |
| Country: Number of subjects enrolled | Turkey: 105 |
| Country: Number of subjects enrolled | United States: 366 |
| Country: Number of subjects enrolled | Mexico: 138 |
| Country: Number of subjects enrolled | Argentina: 208 |
| Country: Number of subjects enrolled | Australia: 36 |
| Country: Number of subjects enrolled | South Africa: 50 |
| Country: Number of subjects enrolled | Ukraine: 228 |
| Country: Number of subjects enrolled | Korea, Republic of: 74 |
| Country: Number of subjects enrolled | Chile: 213 |
| Country: Number of subjects enrolled | Canada: 43 |
| Country: Number of subjects enrolled | Russian Federation: 172 |
| Country: Number of subjects enrolled | Israel: 9 |
| Country: Number of subjects enrolled | Brazil: 73 |
| Country: Number of subjects enrolled | Taiwan: 7 |
| Country: Number of subjects enrolled | Colombia: 17 |
| Worldwide total number of subjects | 2282 |
| EEA total number of subjects | 383 |

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) | 89 |
| Adults (18-64 years) | 1917 |
| From 65 to 84 years | 276 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was initiated at 365 sites in 27 countries. Subjects who successfully completed treatment in studies DRI12544 (NCT01854047), EFC13579 (NCT02414854), EFC13691 (NCT02528214) and PDY14192 (NCT02573233) were eligible to continue their treatment in this extension study LTS12551.

Pre-assignment

Screening details:

A total of 2282 subjects were enrolled and treated in this extension study.

Period 1

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

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Subjects from DRI12544: Placebo/Dupilumab |

Arm description:

Subjects who completed treatment of placebo (for dupilumab) and post-treatment period in study DRI12544, received a loading dose of dupilumab 600 milligram (mg) on Day 1 followed by a subcutaneous (SC) dose of dupilumab 300 mg every 2 weeks (q2w) for 96 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Dupilumab 300 mg, SC injection q2w in abdomen (avoiding navel and waist areas), the upper thighs, or upper arms (lateral side).

| | |
|------------------|---|
| Arm title | Subjects from DRI12544: Dupilumab/Dupilumab |
|------------------|---|

Arm description:

Subjects who completed the treatment of dupilumab and post-treatment period in study DRI12544, received a loading dose of dupilumab 600 mg on Day 1 followed by a SC dose of dupilumab 300 mg q2w for 96 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Dupilumab 300 mg, SC injection q2w in abdomen (avoiding navel and waist areas), the upper thighs, or upper arms (lateral side).

| | |
|------------------|---|
| Arm title | Subjects from EFC13579: Placebo/Dupilumab |
|------------------|---|

Arm description:

Subjects who completed the treatment of placebo (for dupilumab) in study EFC13579 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those

who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Dupilumab 300 mg, SC injection q2w in abdomen (avoiding navel and waist areas), the upper thighs, or upper arms (lateral side).

| | |
|------------------|---|
| Arm title | Subjects from EFC13579: Dupilumab/Dupilumab |
|------------------|---|

Arm description:

Subjects who completed the treatment for dupilumab in study EFC13579 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Dupilumab 300 mg, SC injection q2w in abdomen (avoiding navel and waist areas), the upper thighs, or upper arms (lateral side).

| | |
|------------------|---|
| Arm title | Subjects from EFC13691: Placebo/Dupilumab |
|------------------|---|

Arm description:

Subjects who completed the treatment of placebo (for dupilumab) in study EFC13691 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with OCS and ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Dupilumab 300 mg, SC injection q2w in abdomen (avoiding navel and waist areas), the upper thighs, or upper arms (lateral side).

| | |
|------------------|---|
| Arm title | Subjects from EFC13691: Dupilumab/Dupilumab |
|------------------|---|

Arm description:

Subjects who completed the treatment of dupilumab in study EFC13691 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with OCS and ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

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

| | |
|--|------------------------|
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Dupilumab 300 mg, SC injection q2w in abdomen (avoiding navel and waist areas), the upper thighs, or upper arms (lateral side).

| | |
|------------------|---|
| Arm title | Subjects from PDY14192: Placebo/Dupilumab |
|------------------|---|

Arm description:

Subjects who completed the treatment of placebo (for dupilumab) in study PDY14192 received a SC dose of dupilumab 300 mg q2w for up to 96 weeks in combination with ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Dupilumab 300 mg, SC injection q2w in abdomen (avoiding navel and waist areas), the upper thighs, or upper arms (lateral side).

| | |
|------------------|---|
| Arm title | Subjects from PDY14192: Dupilumab/Dupilumab |
|------------------|---|

Arm description:

Subjects who completed the treatment of dupilumab in study PDY14192, received a SC dose of dupilumab 300 mg q2w for up to 96 weeks in combination with ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dupilumab |
| Investigational medicinal product code | SAR231893 |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Dupilumab 300 mg, SC injection q2w in abdomen (avoiding navel and waist areas), the upper thighs, or upper arms (lateral side).

| Number of subjects in period 1 | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab |
|--------------------------------|---|---|---|
| | | | |
| Started | 111 | 421 | 517 |
| Completed | 102 | 379 | 465 |
| Not completed | 9 | 42 | 52 |
| Adverse Event | 3 | 19 | 13 |
| Poor compliance to protocol | 1 | 1 | 3 |
| Unspecified | 4 | 22 | 33 |
| Lack of efficacy | 1 | - | 3 |

| Number of subjects in period 1 | Subjects from EFC13579: Dupilumab/Dupilumab | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab |
|--------------------------------|---|---|---|
| | | | |
| Started | 1013 | 97 | 90 |
| Completed | 908 | 83 | 76 |
| Not completed | 105 | 14 | 14 |
| Adverse Event | 32 | 4 | 5 |
| Poor compliance to protocol | 7 | 1 | 1 |
| Unspecified | 64 | 8 | 6 |
| Lack of efficacy | 2 | 1 | 2 |

| Number of subjects in period 1 | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--------------------------------|---|---|
| | | |
| Started | 19 | 14 |
| Completed | 15 | 11 |
| Not completed | 4 | 3 |
| Adverse Event | 1 | 2 |
| Poor compliance to protocol | - | - |
| Unspecified | 2 | 1 |
| Lack of efficacy | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|---|
| Reporting group title | Subjects from DRI12544: Placebo/Dupilumab |
| Reporting group description: Subjects who completed treatment of placebo (for dupilumab) and post-treatment period in study DRI12544, received a loading dose of dupilumab 600 milligram (mg) on Day 1 followed by a subcutaneous (SC) dose of dupilumab 300 mg every 2 weeks (q2w) for 96 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from DRI12544: Dupilumab/Dupilumab |
| Reporting group description: Subjects who completed the treatment of dupilumab and post-treatment period in study DRI12544, received a loading dose of dupilumab 600 mg on Day 1 followed by a SC dose of dupilumab 300 mg q2w for 96 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from EFC13579: Placebo/Dupilumab |
| Reporting group description: Subjects who completed the treatment of placebo (for dupilumab) in study EFC13579 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from EFC13579: Dupilumab/Dupilumab |
| Reporting group description: Subjects who completed the treatment for dupilumab in study EFC13579 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from EFC13691: Placebo/Dupilumab |
| Reporting group description: Subjects who completed the treatment of placebo (for dupilumab) in study EFC13691 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with OCS and ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from EFC13691: Dupilumab/Dupilumab |
| Reporting group description: Subjects who completed the treatment of dupilumab in study EFC13691 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with OCS and ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from PDY14192: Placebo/Dupilumab |
| Reporting group description: Subjects who completed the treatment of placebo (for dupilumab) in study PDY14192 received a SC dose of dupilumab 300 mg q2w for up to 96 weeks in combination with ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from PDY14192: Dupilumab/Dupilumab |
| Reporting group description: Subjects who completed the treatment of dupilumab in study PDY14192, received a SC dose of dupilumab 300 mg q2w for up to 96 weeks in combination with ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |

| Reporting group values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab |
|------------------------------------|---|---|---|
| Number of subjects | 111 | 421 | 517 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------|--------|--------|
| Age continuous Units: years | | | |
| arithmetic mean | 49.1 | 49.8 | 48.2 |
| standard deviation | ± 12.3 | ± 12.5 | ± 15.1 |
| Gender categorical Units: Subjects | | | |
| Female | 69 | 259 | 335 |
| Male | 42 | 162 | 182 |
| Race Units: Subjects | | | |
| Caucasian/White | 88 | 339 | 445 |
| Black/of African descent | 1 | 8 | 17 |
| Asian/Oriental | 18 | 70 | 51 |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 0 |
| Other | 4 | 3 | 4 |

| Reporting group values | Subjects from EFC13579: Dupilumab/Dupilumab | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab |
|------------------------------------|---|---|---|
| Number of subjects | 1013 | 97 | 90 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|--------|--------|--------|
| Age continuous Units: years | | | |
| arithmetic mean | 47.9 | 51.3 | 51.7 |
| standard deviation | ± 15.2 | ± 12.4 | ± 12.9 |
| Gender categorical Units: Subjects | | | |
| Female | 618 | 57 | 53 |
| Male | 395 | 40 | 37 |
| Race Units: Subjects | | | |
| Caucasian/White | 844 | 91 | 86 |
| Black/of African descent | 43 | 1 | 2 |
| Asian/Oriental | 116 | 1 | 0 |
| American Indian or Alaska Native | 0 | 2 | 0 |
| Native Hawaiian or Other Pacific Islander | 1 | 0 | 1 |
| Other | 9 | 2 | 1 |

| Reporting group values | Subjects from PDY14192: | Subjects from PDY14192: | Total |
|------------------------|----------------------------|----------------------------|-------|
|------------------------|----------------------------|----------------------------|-------|

| | Placebo/Dupilumab | Dupilumab/Dupiluma b | |
|---|-------------------|-------------------------|------|
| Number of subjects | 19 | 14 | 2282 |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 41.8 ± 10.6 | 44.9 ± 10.8 | - |
| Gender categorical Units: Subjects | | | |
| Female | 7 | 10 | 1408 |
| Male | 12 | 4 | 874 |
| Race Units: Subjects | | | |
| Caucasian/White | 17 | 12 | 1922 |
| Black/of African descent | 2 | 1 | 75 |
| Asian/Oriental | 0 | 1 | 257 |
| American Indian or Alaska Native | 0 | 0 | 2 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 3 |
| Other | 0 | 0 | 23 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Subjects from DRI12544: Placebo/Dupilumab |
| Reporting group description: Subjects who completed treatment of placebo (for dupilumab) and post-treatment period in study DRI12544, received a loading dose of dupilumab 600 milligram (mg) on Day 1 followed by a subcutaneous (SC) dose of dupilumab 300 mg every 2 weeks (q2w) for 96 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from DRI12544: Dupilumab/Dupilumab |
| Reporting group description: Subjects who completed the treatment of dupilumab and post-treatment period in study DRI12544, received a loading dose of dupilumab 600 mg on Day 1 followed by a SC dose of dupilumab 300 mg q2w for 96 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from EFC13579: Placebo/Dupilumab |
| Reporting group description: Subjects who completed the treatment of placebo (for dupilumab) in study EFC13579 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from EFC13579: Dupilumab/Dupilumab |
| Reporting group description: Subjects who completed the treatment for dupilumab in study EFC13579 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from EFC13691: Placebo/Dupilumab |
| Reporting group description: Subjects who completed the treatment of placebo (for dupilumab) in study EFC13691 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with OCS and ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from EFC13691: Dupilumab/Dupilumab |
| Reporting group description: Subjects who completed the treatment of dupilumab in study EFC13691 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with OCS and ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from PDY14192: Placebo/Dupilumab |
| Reporting group description: Subjects who completed the treatment of placebo (for dupilumab) in study PDY14192 received a SC dose of dupilumab 300 mg q2w for up to 96 weeks in combination with ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |
| Reporting group title | Subjects from PDY14192: Dupilumab/Dupilumab |
| Reporting group description: Subjects who completed the treatment of dupilumab in study PDY14192, received a SC dose of dupilumab 300 mg q2w for up to 96 weeks in combination with ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication. | |

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

| | |
|-----------------|--|
| End point title | Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) ^[1] |
|-----------------|--|

End point description:

An Adverse Event (AE) was any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have causal relationship with treatment. TEAEs were defined as AEs that developed, worsened, or became serious during the treatment emergent AE period (time from first dose of investigational medicinal product [IMP] in LTS12551 up to the last dose of dupilumab plus 12 weeks). A Serious AE (SAE) was any untoward medical occurrence that at any dose: 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. Analysis was performed on exposed population which included subjects who actually received at least 1 dose or part of a dose of the IMP.

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

End point timeframe:

From the first IMP injection in LTS12551 to the last IMP injection plus 12 weeks (up to 108 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 endpoint was descriptive in nature, hence no statistical analysis was provided.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| Any TEAE | 88 | 369 | 414 | 789 |
| Any treatment emergent SAE | 14 | 42 | 48 | 106 |
| Any TEAE leading to death | 0 | 3 | 0 | 1 |
| Any TEAE led to permanent treatment discontinuation | 3 | 19 | 12 | 31 |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| Any TEAE | 74 | 70 | 18 | 13 |
| Any treatment emergent SAE | 12 | 10 | 0 | 4 |
| Any TEAE leading to death | 0 | 0 | 0 | 0 |
| Any TEAE led to permanent treatment discontinuation | 4 | 5 | 1 | 2 |

Statistical analyses

Secondary: Number of Subjects With Potentially Clinically Significant Vital Signs Abnormalities During the TEAE Period

| | |
|-----------------|---|
| End point title | Number of Subjects With Potentially Clinically Significant Vital Signs Abnormalities During the TEAE Period |
|-----------------|---|

End point description:

Criteria for potentially clinically significant vital sign abnormalities:

- Systolic blood pressure (SBP): Less than or equal to (\leq) 95 millimetres of mercury (mmHg) and decrease from baseline (DFB) greater than or equal to (\geq) 20 mmHg; \geq 160 mmHg and increase from baseline (IFB) \geq 20 mmHg
- Diastolic blood pressure (DBP): \leq 45 mmHg and DFB \geq 10 mmHg; \geq 110 mmHg and IFB \geq 10 mmHg
- Heart rate (HR): \leq 50 beats per minute (bpm) and DFB \geq 20 bpm; \geq 120 bpm and IFB \geq 20 bpm
- Respiratory rate (RR): less than ($<$) 12 breaths/min(b/m); greater than ($>$) 20 b/m
- Weight (Wt.) (kg): \geq 5 percent (%) DFB; \geq 5% IFB
- Temperature (T): \geq 38.0 degree Celsius ($^{\circ}$ C) rectal/ear/temporal; \geq 37.5 $^{\circ}$ C oral; \geq 37.2 $^{\circ}$ C axillary.

Analysis was performed on exposed population. Here, 'n'=subjects with available data for each specified category.

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

End point timeframe:

From the first IMP injection in LTS12551 to the last IMP injection plus 12 weeks (up to 108 weeks)

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| SBP: \leq 95&DFB \geq 20mmHg(n=111,421,516,1013,97,90,19,14) | 4 | 12 | 19 | 40 |
| SBP \geq 160&IFB \geq 20mmHg(n=111,421,516,1013,97,90,19,14) | 2 | 17 | 21 | 45 |
| DBP: \leq 45&DFB \geq 10mmHg(n=111,421,516,1013,97,90,19,14) | 1 | 1 | 11 | 15 |
| DBP \geq 110&IFB \geq 10mmHg(n=111,421,516,1013,97,90,19,14) | 0 | 4 | 15 | 20 |
| HR: \leq 50&DFB \geq 20bpm(n=111,421,516,1013,97,90,19,14) | 0 | 3 | 2 | 12 |
| HR: \geq 120&IFB \geq 20bpm(n=111,421,516,1013,97,90,19,14) | 0 | 0 | 2 | 5 |
| RR: $<$ 12 b/m(n=111,421,516,1013,97,90,19,14) | 5 | 17 | 18 | 24 |
| RR: $>$ 20 b/m(n=111,421,516,1013,97,90,19,14) | 23 | 104 | 88 | 195 |
| Wt.: \geq 5% DFB (n=111,421,516,1013,97,90,19,14) | 32 | 106 | 146 | 261 |
| Wt.: \geq 5% IFB(n=111,421,485,958;96,89,19,14) | 45 | 181 | 189 | 378 |
| T: \geq 38.0 $^{\circ}$ C(n=111,421,516,1013,97,90,19,14) | 0 | 0 | 1 | 1 |
| T: \geq 37.5 $^{\circ}$ C(n=111,421,516,1013,97,90,19,14) | 1 | 0 | 9 | 6 |
| T: \geq 37.2 $^{\circ}$ C(n=111,421,516,1013,97,90,19,14) | 3 | 21 | 4 | 16 |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| SBP: ≤95&DFB ≥20mmHg(n=111,421,516,1013,97,90,19,14) | 0 | 1 | 2 | 0 |
| SBP ≥160&IFB ≥20mmHg(n=111,421,516,1013,97,90,19,14) | 6 | 1 | 1 | 3 |
| DBP: ≤45&DFB ≥10mmHg(n=111,421,516,1013,97,90,19,14) | 0 | 0 | 0 | 0 |
| DBP ≥110&IFB ≥10mmHg(n=111,421,516,1013,97,90,19,14) | 2 | 0 | 0 | 0 |
| HR: ≤50&DFB ≥20bpm(n=111,421,516,1013,97,90,19,14) | 0 | 0 | 0 | 0 |
| HR: ≥120&IFB ≥20bpm(n=111,421,516,1013,97,90,19,14) | 1 | 0 | 0 | 0 |
| RR: <12 b/m(n=111,421,516,1013,97,90,19,14) | 4 | 0 | 2 | 3 |
| RR: >20 b/m(n=111,421,516,1013,97,90,19,14) | 18 | 12 | 4 | 0 |
| Wt.: ≥5% DFB (n=111,421,516,1013,97,90,19,14) | 22 | 29 | 3 | 3 |
| Wt.: ≥5% IFB(n=111,421,485,958;96,89,19,14) | 29 | 37 | 8 | 5 |
| T: ≥38.0°C(n=111,421,516,1013,97,90,19,14) | 0 | 0 | 0 | 0 |
| T: ≥37.5°C(n=111,421,516,1013,97,90,19,14) | 0 | 0 | 0 | 0 |
| T: ≥37.2°C(n=111,421,516,1013,97,90,19,14) | 0 | 1 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Haematological Parameters (Red blood cells [RBCs], Platelets and Coagulation) During the TEAE Period

| | |
|-----------------|---|
| End point title | Number of Subjects With Potentially Clinically Significant Laboratory Abnormalities: Haematological Parameters (Red blood cells [RBCs], Platelets and Coagulation) During the TEAE Period |
|-----------------|---|

End point description:

Criteria for potentially clinically significant abnormalities:

- Haemoglobin (Hb): ≤ 115 grams per litre (g/L)(Male [M]), 95 g/L (Female[F]); ≥ 185 g/L, 165 g/L (Female); DFB ≥ 20 g/L
- Haematocrit (Hc): ≤ 0.37 volume/volume (v/v) (M); ≤ 0.32 v/v (F); ≥ 0.55 v/v (M); 0.5 v/v (F)
- RBCs: ≥ 6 Tera/L
- Platelets: < 100 Giga(G)/L; ≥ 700 G/L

Analysis was performed on exposed population. Here, 'n'=subjects with available data for each specified

category.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From the first IMP injection in LTS12551 to the last IMP injection plus 12 weeks (up to 108 weeks) | |

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| Hb: ≤115g/L, ≤95g/L (n=111,421,514,1009,97,90,19,14) | 2 | 7 | 12 | 29 |
| Hb: ≥185g/L, ≥165g/L (n=111,421,514,1009,97,90,19,14) | 1 | 3 | 8 | 4 |
| Hb: DFB ≥20 g/L (n=111,421,513,1008,97,90,19,14) | 13 | 41 | 40 | 118 |
| Hc: ≤0.37; ≤0.32v/v (n=111,421,514,1007,97,90,19,14) | 6 | 19 | 23 | 47 |
| Hc: ≥0.55; ≥0.5v/v (n=111,421,514,1007,97,90,19,14) | 3 | 6 | 26 | 36 |
| RBCs: ≥6 Tera/L (n=111,421,514,1009,97,90,19,14) | 1 | 5 | 28 | 15 |
| Platelets: <100G/L (n=111,421,514,1007,97,90,19,14) | 0 | 2 | 2 | 1 |
| Platelets: ≥700G/L (n=111,421,514,1007,97,90,19,14) | 0 | 1 | 1 | 0 |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| Hb: ≤115g/L, ≤95g/L (n=111,421,514,1009,97,90,19,14) | 0 | 3 | 0 | 0 |
| Hb: ≥185g/L, ≥165g/L (n=111,421,514,1009,97,90,19,14) | 2 | 1 | 0 | 0 |
| Hb: DFB ≥20 g/L (n=111,421,513,1008,97,90,19,14) | 11 | 7 | 0 | 0 |
| Hc: ≤0.37; ≤0.32v/v (n=111,421,514,1007,97,90,19,14) | 3 | 5 | 0 | 0 |
| Hc: ≥0.55; ≥0.5v/v (n=111,421,514,1007,97,90,19,14) | 3 | 3 | 0 | 1 |
| RBCs: ≥6 Tera/L (n=111,421,514,1009,97,90,19,14) | 0 | 2 | 0 | 1 |
| Platelets: <100G/L (n=111,421,514,1007,97,90,19,14) | 1 | 0 | 0 | 1 |

| | | | | |
|---|---|---|---|---|
| Platelets: $\geq 700\text{G/L}$ (n=111,421,514,1007, 97,90,19,14) | 0 | 0 | 0 | 0 |
|---|---|---|---|---|

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Severe Exacerbation Events During the Treatment Period

| | |
|--|--|
| End point title | Number of Severe Exacerbation Events During the Treatment Period |
| End point description: Severe asthma exacerbation events were defined as a deterioration of asthma which required: use of systemic corticosteroids for ≥ 3 days, (subjects from study EFC13691, and who were taking systemic corticosteroids: the use of systemic corticosteroids at least double the current dose and for ≥ 3 days.) or, hospitalisation or emergency room visit because of asthma, required systemic corticosteroids. Analysis was performed on exposed population. | |
| End point type | Secondary |
| End point timeframe: From the first IMP injection in LTS12551 to the last IMP injection plus 2 weeks (up to 96 weeks) | |

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|-----------------------------|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: number of events | | | | |
| number (not applicable) | 62 | 242 | 234 | 437 |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|-----------------------------|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: number of events | | | | |
| number (not applicable) | 35 | 41 | 3 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Annualised Event Rate Per Subject-Years for Severe Exacerbation During

The Treatment Period

| | |
|-----------------|---|
| End point title | Annualised Event Rate Per Subject-Years for Severe Exacerbation During The Treatment Period |
|-----------------|---|

End point description:

The annualised event rate per subject-years was defined as the total number of events that occurred during the treatment period divided by the total number of subject-years during the treatment period. Analysis was performed on exposed population.

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

End point timeframe:

From the first IMP injection in LTS12551 to the last IMP injection plus 2 weeks (up to 96 weeks)

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: exacerbation events per subject-years | | | | |
| number (not applicable) | 0.314 | 0.330 | 0.351 | 0.331 |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: exacerbation events per subject-years | | | | |
| number (not applicable) | 0.302 | 0.391 | 0.149 | 0.077 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Expiratory Volume in 1 Second (FEV1) at Weeks 48 and 96

| | |
|-----------------|--|
| End point title | Change From Baseline in Forced Expiratory Volume in 1 Second (FEV1) at Weeks 48 and 96 |
|-----------------|--|

End point description:

FEV1 was the volume of air exhaled in the first second of a forced expiration as measured by spirometer. For this analysis, baseline was defined as parent study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48 and Week 96 of this extension study

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: litres | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=105,396,486, 951,88,82,16,11) | 0.24 (± 0.42) | 0.28 (± 0.45) | 0.34 (± 0.44) | 0.36 (± 0.53) |
| Week 96 (n=102,380,219,447,32,28,5,2) | 0.22 (± 0.44) | 0.27 (± 0.46) | 0.33 (± 0.44) | 0.31 (± 0.47) |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: litres | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=105,396,486, 951,88,82,16,11) | 0.31 (± 0.50) | 0.33 (± 0.53) | 0.23 (± 0.40) | 0.01 (± 0.21) |
| Week 96 (n=102,380,219,447,32,28,5,2) | 0.36 (± 0.66) | 0.25 (± 0.46) | 0.14 (± 0.41) | 0.01 (± 0.12) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percent Predicted FEV1 at Weeks 48 and 96

| | |
|-----------------|---|
| End point title | Change From Baseline in Percent Predicted FEV1 at Weeks 48 and 96 |
|-----------------|---|

End point description:

FEV1 was the volume of air exhaled in the first second of a forced expiration as measured by spirometer. For this analysis, baseline was defined as parent study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48 and Week 96 of this extension study

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: percent predicted FEV1 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=105,396,486, 951,88,82,16,11) | 9.21 (± 13.61) | 10.42 (± 14.61) | 11.74 (± 14.27) | 12.16 (± 16.58) |
| Week 96 (n=102,380,219,447,32,28,5,2) | 8.86 (± 14.47) | 10.68 (± 15.10) | 12.53 (± 14.50) | 11.25 (± 14.55) |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: percent predicted FEV1 | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=105,396,486, 951,88,82,16,11) | 10.45 (± 15.03) | 12.41 (± 18.27) | 5.88 (± 10.06) | 1.36 (± 8.35) |
| Week 96 (n=102,380,219,447,32,28,5,2) | 13.06 (± 19.57) | 10.00 (± 15.79) | 4.20 (± 9.60) | 2.00 (± 2.83) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity (FVC) at Weeks 48 and 96

| | |
|-----------------|--|
| End point title | Change From Baseline in Forced Vital Capacity (FVC) at Weeks 48 and 96 |
|-----------------|--|

End point description:

FVC was a standard pulmonary function test used to quantify respiratory muscle weakness. FVC was the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. For this analysis, baseline was defined as parent study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48, and Week 96 of this extension study

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: litres | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=105,396,486, 951,88,82,16,11) | 0.22 (± 0.45) | 0.25 (± 0.50) | 0.30 (± 0.48) | 0.35 (± 0.60) |
| Week 96 (n=102,380,219,447,32,28,5,2) | 0.16 (± 0.47) | 0.22 (± 0.52) | 0.27 (± 0.48) | 0.25 (± 0.50) |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: litres | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=105,396,486, 951,88,82,16,11) | 0.29 (± 0.56) | 0.38 (± 0.56) | 0.21 (± 0.42) | 0.05 (± 0.30) |
| Week 96 (n=102,380,219,447,32,28,5,2) | 0.38 (± 0.82) | 0.22 (± 0.42) | 0.08 (± 0.29) | 0.05 (± 0.40) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Expiratory Flow (FEF) 25-75% at Weeks 48 and 96

| | |
|-----------------|--|
| End point title | Change From Baseline in Forced Expiratory Flow (FEF) 25-75% at Weeks 48 and 96 |
|-----------------|--|

End point description:

FEF was the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation. FEF 25-75% was defined as the mean FEF between 25% and 75% of the FVC, where FVC was defined as the volume of air that can forcibly be blown out after full inspiration in the upright position, measured in liters. For this analysis, baseline was defined as parent study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48, and Week 96 of this extension study

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: litres/second | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=105,396,486, 951,88,82,16,11) | 0.27 (± 0.55) | 0.31 (± 0.55) | 0.39 (± 0.57) | 0.39 (± 0.66) |
| Week 96 (n=102,380,219,447,32,28,5,2) | 0.28 (± 0.57) | 0.32 (± 0.55) | 0.38 (± 0.53) | 0.36 (± 0.61) |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: litres/second | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=105,396,486, 951,88,82,16,11) | 0.34 (± 0.56) | 0.29 (± 0.66) | 0.23 (± 0.44) | 0.04 (± 0.26) |
| Week 96 (n=102,380,219,447,32,28,5,2) | 0.42 (± 0.64) | 0.27 (± 0.53) | 0.19 (± 0.41) | 0.04 (± 0.14) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Asthma Control Questionnaire 5-Question Version (ACQ-5) Mean Scores at Weeks 24 and 48

| | |
|-----------------|--|
| End point title | Change From Baseline in Asthma Control Questionnaire 5-Question Version (ACQ-5) Mean Scores at Weeks 24 and 48 |
|-----------------|--|

End point description:

The ACQ-5 has 5 questions, reflecting the top-scoring five asthma symptoms: woken at night by symptoms, wake in the mornings with symptoms, limitation of daily activities, shortness of breath and wheeze. Subjects were asked to recall how their asthma had been during the previous week and to respond to each of the five symptom questions on a 7-point scale ranged from 0 (no impairment) to 6 (maximum impairment). ACQ-5 total mean score was mean of the scores of all 5 questions and, therefore, ranged from 0 (totally controlled) to 6 (severely uncontrolled), higher scores indicated lower asthma control. For this analysis, baseline was defined as the parent study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Weeks 24, and 48 of this extension study

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 (n=110, 421, 513, 1005, 96, 87, 19, 13) | -1.37 (± 0.91) | -1.48 (± 1.10) | 1.61 (± 1.08) | -1.68 (± 1.05) |
| Week 48 (n= 105, 400, 488, 957, 90, 78, 15, 11) | -1.33 (± 1.07) | -1.57 (± 1.11) | -1.64 (± 1.08) | -1.69 (± 1.08) |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 (n=110, 421, 513, 1005, 96, 87, 19, 13) | -1.09 (± 1.10) | -1.15 (± 1.17) | -0.96 (± 1.03) | -0.80 (± 0.46) |
| Week 48 (n= 105, 400, 488, 957, 90, 78, 15, 11) | -1.21 (± 1.00) | -1.06 (± 1.25) | -0.89 (± 1.02) | -0.87 (± 0.58) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving ACQ-5 Score Response (ACQ-5 Responders) at Weeks 24 and 48

| | |
|-----------------|---|
| End point title | Percentage of Subjects Achieving ACQ-5 Score Response (ACQ-5 Responders) at Weeks 24 and 48 |
|-----------------|---|

End point description:

ACQ-5 response was defined as change from baseline in ACQ-5 scores ≥ 0.5 . The ACQ-5 has 5 questions, reflecting the top-scoring five asthma symptoms: woken at night by symptoms, wake in the mornings with symptoms, limitation of daily activities, shortness of breath and wheeze. Subjects were asked to recall how their asthma had been during the previous week and to respond to each of the five symptom questions on a 7-point scale ranged from 0 (no impairment) to 6 (maximum impairment). ACQ-5 mean total score was mean of the scores of all 5 questions and, therefore, ranged from 0 (totally controlled) to 6 (severely uncontrolled). Higher score indicated lower asthma control. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

At Weeks 24, and 48 of this extension study

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 24 (n=110, 421,513, 1005,96, 87,19, 13) | 82.7 | 80.8 | 84.0 | 86.5 |
| Week 48 (n=105,400,488, 957, 90, 78,15, 11) | 79.0 | 82.3 | 85.7 | 86.7 |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 24 (n=110, 421,513, 1005,96, 87,19, 13) | 67.7 | 70.1 | 57.9 | 69.2 |
| Week 48 (n=105,400,488, 957, 90, 78,15, 11) | 75.6 | 70.5 | 60.0 | 72.7 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Asthma Quality of Life Questionnaire (AQLQ) Global Scores at Weeks 24 and 48

| | |
|-----------------|---|
| End point title | Change From Baseline in Asthma Quality of Life Questionnaire (AQLQ) Global Scores at Weeks 24 and 48 ^[2] |
|-----------------|---|

End point description:

The AQLQ was designed to measure the functional impairments that are most troublesome to adults as a result of their asthma. The AQLQ comprises of 32 items in 4 domains: symptoms (12 items), activity limitation (11 items), emotional function (5 items), and environmental stimuli (4 items). Each item was scored on a 7-point likert scale ranged from 1=severely impaired to 7=not impaired. The 32 items of the questionnaire were averaged to produce one overall quality of life score ranging from 1 (severely impaired) to 7 (not impaired); higher scores indicated better quality of life. For this analysis, baseline was defined as the parent study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Weeks 24, and 48 of this extension study

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data was planned to be collected and analysed for the subjects from Studies DRI12544, EFC13579, and EFC13691 only.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 (n= 108,413,495, 948, 95, 98) | 1.07 (± 0.99) | 1.28 (± 1.24) | 1.38 (± 1.15) | 1.38 (± 1.16) |
| Week 48 (n= 103, 397, 473, 908, 90, 79) | 1.07 (± 1.13) | 1.40 (± 1.19) | 1.39 (± 1.17) | 1.40 (± 1.18) |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 97 | 90 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 (n= 108,413,495, 948, 95, 98) | 0.99 (± 1.10) | 0.97 (± 1.26) | | |
| Week 48 (n= 103, 397, 473, 908, 90, 79) | 1.06 (± 0.98) | 1.00 (± 1.23) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving AQLQ Global Score Response (AQLQ Responders) at Weeks 24 and 48

| | |
|-----------------|---|
| End point title | Percentage of Subjects Achieving AQLQ Global Score Response (AQLQ Responders) at Weeks 24 and 48 ^[3] |
|-----------------|---|

End point description:

AQLQ global response was defined as subjects with change from baseline in AQLQ global score ≥ 0.5 . The AQLQ was designed to measure the functional impairments that are most troublesome to adults as a result of their asthma. The AQLQ comprises of 32 items in 4 domains: symptoms (12 items), activity limitation (11 items), emotional function (5 items), environmental stimuli (4 items). Each item is scored on a 7-point likert scale (1=severely impaired, 7=not impaired). The 32 items of the questionnaire are averaged to produce one overall quality of life score ranging from 1 (severely impaired) to 7 (not impaired). Higher scores indicated better quality of life. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

At Weeks 24, and 48 of this extension study

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data was planned to be collected and analysed for the subjects from Studies DRI12544, EFC13579, and EFC13691 only.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|-----------------------------------|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 24 (n=108,413,495,948,95,88) | 67.6 | 73.6 | 77.6 | 77.2 |
| Week 48 (n=103,397,473,908,90,79) | 65.0 | 76.3 | 77.4 | 78.4 |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 97 | 90 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 24 (n=108,413,495,948,95,88) | 64.2 | 61.4 | | |
| Week 48 (n=103,397,473,908,90,79) | 73.3 | 68.4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Dupilumab Over Time Till Week 96

| | |
|-----------------|--|
| End point title | Serum Concentrations of Dupilumab Over Time Till Week 96 |
|-----------------|--|

End point description:

For this analysis, baseline was defined as the parent study baseline. Analysis was performed on Pharmacokinetics (PK) population which consisted of all the subjects who had actually received at least one dose or part of a dose of dupilumab in the LTS12551 study, with at least one non-missing and evaluable pre-dose serum concentration value after the first dose of dupilumab in the LTS12551 study. Here, 'n'=subjects with available data for each specified category and '99999' represented that data was not calculated for specified category due to none of the evaluable subjects.

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

End point timeframe:

Baseline of parent study, Weeks 0, 4, 12, 24, 48, 72, and 96 of this extension study

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1008 |
| Units: nanogram per millilitre | | | | |
| geometric mean (geometric coefficient of variation) | | | | |

| | | | | |
|--|---------------------|---------------------|---------------------|---------------------|
| Baseline (n=110,413,0,993,0,88,0,14) | 0.00 (± 0.000) | 0.00 (± 1990.640) | 99999 (± 99999) | 0.00 (± 2286.888) |
| Week 0 (n=110,417,0,968,0,88,0,14) | 0.00 (± 0.000) | 0.00 (± 0.000) | 37230.97 (± 73.261) | 37230.97 (± 73.261) |
| Week 4 (n=109,414,500,971,93,88,18,13) | 46848.70 (± 43.149) | 40704.77 (± 47.293) | 25847.86 (± 49.371) | 50566.66 (± 55.104) |
| Week 12 (n=111,417,501,973,94,87,16,12) | 54467.13 (± 50.267) | 48155.26 (± 52.353) | 45406.55 (± 51.399) | 55140.49 (± 53.114) |
| Week 24 (n=108,405,500,973,90,83,16,11) | 47023.84 (± 51.645) | 49730.56 (± 53.625) | 50984.57 (± 53.744) | 54897.58 (± 54.044) |
| Week 48 (n=106,397,484,951,89,82,16,11) | 46355.26 (± 52.612) | 45919.75 (± 55.932) | 41867.50 (± 60.345) | 41849.96 (± 62.049) |
| Week 72 (n=105,385,227,453,35,29,5,2) | 44771.52 (± 56.256) | 46842.64 (± 53.335) | 45628.10 (± 56.232) | 46372.55 (± 57.719) |
| Week 96 (n=101,381,222,446,33,29,5,2) | 42431.08 (± 59.222) | 42661.18 (± 59.658) | 38908.58 (± 64.633) | 39088.60 (± 62.897) |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 96 | 90 | 19 | 14 |
| Units: nanogram per millilitre | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Baseline (n=110,413,0,993,0,88,0,14) | 99999 (± 99999) | 0.00 (± 0.000) | 99999 (± 99999) | 0.00 (± 0.000) |
| Week 0 (n=110,417,0,968,0,88,0,14) | 99999 (± 99999) | 40754.49 (± 54.858) | 99999 (± 99999) | 52545.41 (± 44.678) |
| Week 4 (n=109,414,500,971,93,88,18,13) | 25868.25 (± 53.450) | 48295.93 (± 52.655) | 23336.89 (± 50.542) | 56486.58 (± 45.755) |
| Week 12 (n=111,417,501,973,94,87,16,12) | 44064.95 (± 57.100) | 50904.34 (± 51.233) | 49026.51 (± 41.619) | 55365.35 (± 53.317) |
| Week 24 (n=108,405,500,973,90,83,16,11) | 57363.72 (± 57.889) | 44219.42 (± 55.383) | 63080.82 (± 51.224) | 60643.16 (± 41.617) |
| Week 48 (n=106,397,484,951,89,82,16,11) | 36219.47 (± 67.530) | 36564.41 (± 60.959) | 24864.79 (± 58.016) | 53320.11 (± 46.714) |
| Week 72 (n=105,385,227,453,35,29,5,2) | 60117.76 (± 62.390) | 32029.19 (± 66.785) | 40362.88 (± 55.567) | 26383.90 (± 120.013) |
| Week 96 (n=101,381,222,446,33,29,5,2) | 49810.65 (± 65.546) | 19030.70 (± 67.237) | 42360.37 (± 49.409) | 56378.01 (± 7.140) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Antidrug Antibodies (ADA) Response

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Antidrug Antibodies (ADA) Response |
|-----------------|--|

End point description:

ADA response were categorised as: treatment emergent and treatment boosted response. 1) Treatment emergent was defined as an ADA positive response in the assay post first dose, when baseline results were negative or missing. 2) Treatment boosted was defined as: an ADA positive response in the assay

post first dose that was greater-than or equal to 4-fold over baseline titer levels, when baseline results were positive. The criteria for positive was defined as "30 to > 10,000", where low titer (< 1,000); moderate (1,000 ≤ titer ≤ 10,000) and high titer (> 10,000). Analysis was performed on ADA population which consisted of all subjects who had actually received at least one dose or part of a dose of dupilumab in the LTS12551 study, with at least one pre-dose sample that was assayed successfully using the ADA assay after the first dose of dupilumab in the LTS12551 study.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From the first IMP injection in LTS12551 to the last IMP injection plus 2 weeks (up to 96 weeks) | |

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|-------------------------------|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 515 | 1008 |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Treatment-emergent ADA | 10.8 | 12.1 | 9.5 | 4.5 |
| Treatment-boosted ADA | 0 | 0 | 0 | 0 |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|-------------------------------|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 95 | 90 | 19 | 14 |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Treatment-emergent ADA | 7.4 | 8.9 | 0 | 7.1 |
| Treatment-boosted ADA | 1.1 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Blood Eosinophils Cells Count at Weeks 48 and 96

| | |
|--|--|
| End point title | Change From Baseline in Blood Eosinophils Cells Count at Weeks 48 and 96 |
| End point description: | |
| For this analysis, baseline was defined as parent study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline of parent study, Week 48 and Week 96 of this extension study | |

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab | Subjects from EFC13579: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 111 | 421 | 517 | 1013 |
| Units: giga per litre | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=103,386,474, 935,87,82,14,10) | 0.007 (± 0.475) | -0.041 (± 0.588) | -0.096 (± 0.428) | -0.099 (± 0.360) |
| Week 96 (n=102,381,218,435,30,29,4,2) | -0.074 (± 0.251) | -0.081 (± 0.562) | -0.161 (± 0.391) | -0.114 (± 0.354) |

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab |
|--|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 97 | 90 | 19 | 14 |
| Units: giga per litre | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=103,386,474, 935,87,82,14,10) | 0.098 (± 0.450) | 0.016 (± 0.382) | -0.066 (± 0.181) | -0.026 (± 0.187) |
| Week 96 (n=102,381,218,435,30,29,4,2) | -0.051 (± 0.399) | 0.083 (± 0.642) | -0.103 (± 0.039) | 0.025 (± 0.134) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Morning Peak Expiratory Flow (PEF) at Weeks 48 and 96- Subject From Study DRI12544

| | |
|-----------------|---|
| End point title | Change From Baseline in Morning Peak Expiratory Flow (PEF) at Weeks 48 and 96- Subject From Study DRI12544 ^[4] |
|-----------------|---|

End point description:

The PEF was a subject's maximum speed of expiration, as measured with a peak flow meter. Peak flow testing for PEF was performed at morning and evening. Morning PEF was performed within 15 minutes after arising (between 5:30 AM and 10 AM) prior to taking any salbutamol/albuterol or levosalbutamol/levalbuterol. For this analysis, baseline was defined as parent study DRI12544 baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48 and Week 96 of this extension study

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data was planned to be collected and analysed only for the subjects from Study DRI12544 and not for the subjects from other studies.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 421 | | |
| Units: litres per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=110,407) | 13.26 (\pm 76.71) | 22.95 (\pm 70.06) | | |
| Week 96 (n=92,340) | 13.63 (\pm 83.88) | 21.69 (\pm 77.70) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evening Peak Expiratory Flow (PEF) at Weeks 48 and 96- Subjects From Study DRI12544

| | |
|-----------------|--|
| End point title | Change From Baseline in Evening Peak Expiratory Flow (PEF) at Weeks 48 and 96- Subjects From Study DRI12544 ^[5] |
|-----------------|--|

End point description:

The PEF was a subject's maximum speed of expiration, as measured with a peak flow meter. Peak flow testing for PEF was performed at morning and evening. Evening PEF was performed in the evening (between 5:30 PM and 10 PM) prior to taking any salbutamol/albuterol or levosalbutamol/levalbuterol. For this analysis, baseline was defined as parent DRI12544 study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-point.

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

End point timeframe:

Baseline of parent study, Week 48 and Week 96 of this extension study

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be collected and analysed only for the subjects from Study DRI12544 and not for the subjects from other studies.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 421 | | |
| Units: litres per minute | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=109,406) | 4.65 (\pm 75.00) | 11.97 (\pm 72.19) | | |
| Week 96 (n=89,327) | 1.16 (\pm 79.47) | 10.05 (\pm 79.47) | | |

Statistical analyses

Secondary: Change From Baseline in Morning Asthma Symptom Scores at Weeks 48 and 96- Subjects From Study DRI12544

| | |
|-----------------|---|
| End point title | Change From Baseline in Morning Asthma Symptom Scores at Weeks 48 and 96- Subjects From Study DRI12544 ^[6] |
|-----------------|---|

End point description:

Morning asthma symptom score was determined using AM (ante meridiem) symptom scoring system which evaluated subject's overall asthma symptoms experienced during the night. It ranges from 0 to 4 as: 0=no asthma symptoms, slept through the night, 1=slept well, but some complaints in the morning. No nighttime awakenings, 2=woke up once because of asthma (including early awakening), 3=woke up several times because of asthma (including early awakening), 4=bad night, awake most of the night because of asthma; higher scores indicated more severe symptoms. For this analysis, baseline was defined as parent DRI12544 study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48 and Week 96 of this extension study

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data was planned to be collected and analysed only for the subjects from Study DRI12544 and not for the subjects from other studies.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 421 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=110,410) | -0.49 (± 0.78) | -0.68 (± 0.79) | | |
| Week 96 (n=92,324) | -0.52 (± 0.90) | -0.76 (± 0.81) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Evening Asthma Symptom Scores at Weeks 48 and 96- Subjects From Study DRI12544

| | |
|-----------------|---|
| End point title | Change From Baseline in Evening Asthma Symptom Scores at Weeks 48 and 96- Subjects From Study DRI12544 ^[7] |
|-----------------|---|

End point description:

Evening asthma symptom score was determined using PM (post meridiem) symptom scoring system which evaluated subject's overall asthma symptoms experienced during the day. It ranged from 0 to 4 as: 0=very well, no asthma symptoms, 1=one episode of wheezing, cough, or breathlessness, 2=more than one episode of wheezing, cough, or breathlessness without interference of normal activities, 3=wheezing, cough, or breathlessness most of the day, which interfered to some extent with normal activities, 4=asthma very bad, unable to carry out daily activities as usual; higher scores indicated more severe symptoms. For this analysis, baseline was defined as parent DRI12544 study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48, and Week 96 of this extension study

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data was planned to be collected and analysed only for the subjects from Study DRI12544 and not for the subjects from other studies.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 421 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=109,407) | -0.47 (± 0.81) | -0.72 (± 0.85) | | |
| Week 96 (n=88,330) | -0.49 (± 0.94) | -0.79 (± 0.88) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Number of Inhalations Per Day of Salbutamol/Albuterol or Levosalbutamol/Levalbuterol for Symptom Relief at Weeks 48 and 96- Subjects From Study DRI12544

| | |
|-----------------|---|
| End point title | Change From Baseline in Number of Inhalations Per Day of Salbutamol/Albuterol or Levosalbutamol/Levalbuterol for Symptom Relief at Weeks 48 and 96- Subjects From Study DRI12544 ^[8] |
|-----------------|---|

End point description:

The number of salbutamol/albuterol or levosalbutamol/levalbuterol inhalations was recorded daily by the subjects in an electronic diary/PEF meter. Mean number of inhalations in last 7 days prior to each visit was calculated and was used in computation of data reported. For this analysis, baseline was defined as parent DRI12544 study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48, and Week 96 of this extension study

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data was planned to be collected and analysed only for the subjects from Study DRI12544 and not for the subjects from other studies.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 421 | | |
| Units: number of inhalations per day | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=108,406) | -0.00 (± 3.65) | -0.68 (± 4.80) | | |
| Week 96 (n=88,325) | -0.14 (± 4.17) | -0.82 (± 5.18) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Number of Nocturnal Awakenings at Weeks 48 and 96- Subjects From Study DRI12544

| | |
|-----------------|--|
| End point title | Change From Baseline in Number of Nocturnal Awakenings at Weeks 48 and 96- Subjects From Study DRI12544 ^[9] |
|-----------------|--|

End point description:

The number of nocturnal awakening because of asthma symptoms were recorded every morning by the subjects in an electronic diary. Mean number of awakenings in last 7 days prior to each visit was calculated and was used in computation of data reported. For this analysis, baseline was defined as parent DRI12544 study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data for each specified category.

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

End point timeframe:

Baseline of parent study, Week 48 and Week 96 of this extension study

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be collected and analysed only for the subjects from Study DRI12544 and not for the subjects from other studies.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 421 | | |
| Units: nocturnal awakenings | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=110,410) | -0.27 (± 0.54) | -0.43 (± 0.89) | | |
| Week 96 (n=92,344) | -0.29 (± 0.58) | -0.49 (± 0.96) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline in Oral Corticosteroid (OCS) Dose at Weeks 48, and 96- Subjects From Study EFC13691

| | |
|-----------------|--|
| End point title | Percent Change from Baseline in Oral Corticosteroid (OCS) Dose at Weeks 48, and 96- Subjects From Study EFC13691 ^[10] |
|-----------------|--|

End point description:

OCS was allowed as background controller medication for the subjects from study EFC13691 only. For this analysis, baseline was defined as parent study EFC13691 baseline. Analysis was performed on exposed population. Here, 'n' = subjects with available data for each specified category.

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

End point timeframe:

Baseline of parent study, Weeks 48 and 96 of this extension study

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be collected and analysed only for the subjects from Study EFC13691 and not for the subjects from other studies.

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 97 | 90 | | |
| Units: percent change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=77,57) | 55.32 (± 42.98) | 80.23 (± 30.44) | | |
| Week 96 (n=28,19) | 71.37 (± 29.37) | 88.16 (± 26.83) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving a Reduction of 50% or Greater (≥ 50%) in OCS Dose Over Time at Weeks 48 and 96- Subjects From Study EFC13691

| | |
|-----------------|--|
| End point title | Percentage of Subjects Achieving a Reduction of 50% or Greater (≥ 50%) in OCS Dose Over Time at Weeks 48 and 96- Subjects From Study EFC13691 ^[11] |
|-----------------|--|

End point description:

OCS was allowed as background controller medication for the subjects from study EFC13691 only. Percentage of subjects who achieved a reduction of ≥ 50% in OCS dose were reported. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Weeks 48 and 96 of this extension study

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be collected and analysed only for the subjects from Study EFC13691 and not for the subjects from other studies.

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 97 | 90 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 48 (n=77,57) | 64.9 | 86.0 | | |
| Week 96 (n=28,19) | 82.1 | 94.7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Background OCS Completely Tapered off Over Time at Weeks 48 and 96-Subjects From Study EFC13691

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Background OCS Completely Tapered off Over Time at Weeks 48 and 96-Subjects From Study EFC13691 ^[12] |
|-----------------|---|

End point description:

OCS was allowed as background controller medication for the subjects from study EFC13691 only. Number of subjects who gradually discontinued or reduced therapeutic dose were reported in this end-point. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Weeks 48, and 96 of this extension study

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be collected and analysed only for the subjects from Study EFC13691 and not for the subjects from other studies.

| End point values | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 97 | 90 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 48 (n=77,57) | 31.2 | 59.6 | | |
| Week 96 (n=28,19) | 42.9 | 78.9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European-Quality of Life-5 Dimension Instrument-3 Levels (EQ-5D-3L) Index Scores at Weeks 48 and 96- Subject From Study DRI12544

| | |
|-----------------|--|
| End point title | Change From Baseline in European-Quality of Life-5 Dimension Instrument-3 Levels (EQ-5D-3L) Index Scores at Weeks 48 and 96- Subject From Study DRI12544 ^[13] |
|-----------------|--|

End point description:

EQ-5D-3L: validated and reliable self-report health status questionnaire consisted of EQ-5D descriptive

system and visual analogue scale (VAS). EQ-5D descriptive system comprises 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension measured on 3 levels: no problem, some problems, and severe problems. The 5 dimensional 3-level systems was converted into single index utility score, and the score was 0 – 100, where 100=best health state; and 0=worst health state; where higher scores indicated better outcome. For this analysis, baseline was defined as parent DRI12544 study baseline. Analysis performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48 and Week 96 of this extension study

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be collected and analysed only for the subjects from Study DRI12544 and not for the subjects from other studies.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 421 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=100,370) | 0.13 (± 0.20) | 0.14 (± 0.21) | | |
| Week 96 (n=69,294) | 0.12 (± 0.18) | 0.13 (± 0.21) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EQ-5D-3L VAS Scores at Weeks 48 and 96- Subjects From Study DRI12544

| | |
|-----------------|--|
| End point title | Change From Baseline in EQ-5D-3L VAS Scores at Weeks 48 and 96- Subjects From Study DRI12544 ^[14] |
|-----------------|--|

End point description:

EQ-5D VAS was used to record a subject's rating for his/her current health-related quality of life state and captured on a vertical VAS (0-100), where 0=worst imaginable health state and 100=best imaginable health state, where higher states indicated better outcomes. For this analysis, baseline was defined as parent DRI12544 study baseline. Analysis was performed on exposed population. Here, 'n'=subjects with available data at specified time-points.

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

End point timeframe:

Baseline of parent study, Week 48 and Week 96 of this extension study

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be collected and analysed only for the subjects from Study DRI12544 and not for the subjects from other studies.

| End point values | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 111 | 421 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 48 (n=100,370) | 10.10 (± 15.40) | 12.88 (± 18.76) | | |
| Week 96 (n=69,294) | 9.90 (± 18.92) | 13.95 (± 18.81) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from first dose of IMP up to 12 weeks after last dose of IMP (i.e. from Baseline up to Week 108)

Adverse event reporting additional description:

Reported AE and deaths were TEAEs that developed, worsened, or became serious during the TEAE period (time from the first dose of dupilumab in LTS12551 up to the last dose of dupilumab plus 12 weeks) (i.e. up to 108 weeks). Analysis was performed on safety population.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Subjects from DRI12544: Placebo/Dupilumab |
|-----------------------|---|

Reporting group description:

Subjects who completed treatment of placebo (for dupilumab) and post-treatment period in study DRI12544, received a loading dose of dupilumab 600 mg on Day 1 followed by a SC dose of dupilumab 300 mg q2w for 96 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|-----------------------|---|
| Reporting group title | Subjects from DRI12544: Dupilumab/Dupilumab |
|-----------------------|---|

Reporting group description:

Subjects who completed the treatment of dupilumab and post-treatment period in study DRI12544, received a loading dose of dupilumab 600 mg on Day 1 followed by a SC dose of dupilumab 300 mg q2w for 96 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|-----------------------|---|
| Reporting group title | Subjects from EFC13579: Placebo/Dupilumab |
|-----------------------|---|

Reporting group description:

Subjects who completed the treatment of placebo (for dupilumab) in study EFC13579 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|-----------------------|---|
| Reporting group title | Subjects from EFC13579: Dupilumab/Dupilumab |
|-----------------------|---|

Reporting group description:

Subjects who completed the treatment for dupilumab in study EFC13579 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with ICS therapy/LABA therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|-----------------------|---|
| Reporting group title | Subjects from EFC13691: Placebo/Dupilumab |
|-----------------------|---|

Reporting group description:

Subjects who completed the treatment of placebo (for dupilumab) in study EFC13691 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with OCS and ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|-----------------------|---|
| Reporting group title | Subjects from EFC13691: Dupilumab/Dupilumab |
|-----------------------|---|

Reporting group description:

Subjects who completed the treatment of dupilumab in study EFC13691 and, who were enrolled before amendment 4 received a SC dose of dupilumab 300 mg q2w for 96 weeks and those who were enrolled after amendment 4 received a SC dose of dupilumab 300 mg q2w for 48 weeks in combination with OCS and ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|-----------------------|---|
| Reporting group title | Subjects from PDY14192: Placebo/Dupilumab |
|-----------------------|---|

Reporting group description:

Subjects who completed the treatment of placebo (for dupilumab) in study PDY14192 received a SC dose of dupilumab 300 mg q2w for up to 96 weeks in combination with CS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| | |
|-----------------------|---|
| Reporting group title | Subjects from PDY14192: Dupilumab/Dupilumab |
|-----------------------|---|

Reporting group description:

Subjects who completed the treatment of dupilumab in study PDY14192, received a SC dose of dupilumab 300 mg q2w for up to 96 weeks in combination with ICS therapy in this extension study. Salbutamol/albuterol or Levosalbutamol/levalbuterol was given as reliever medication.

| Serious adverse events | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupiluma b | Subjects from EFC13579: Placebo/Dupilumab |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 14 / 111 (12.61%) | 42 / 421 (9.98%) | 48 / 517 (9.28%) |
| number of deaths (all causes) | 0 | 1 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma Gastric | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Adenocarcinoma Of Colon | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign Ovarian Tumour | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bowen's Disease | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Breast Cancer | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 2 / 517 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon Adenoma | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon Cancer | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial Cancer | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibroadenoma Of Breast | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Follicular Thyroid Cancer | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric Adenoma | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hodgkin's Disease | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraductal Proliferative Breast Lesion | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Juvenile Melanoma Benign | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large Intestine Benign Neoplasm | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung Cancer Metastatic | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Metastases To Central Nervous System | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Non-Small Cell Lung Cancer | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteochondroma | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian Cancer | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papillary Thyroid Cancer | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate Cancer | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate Cancer Stage I | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal Cancer | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous Cell Carcinoma Of Skin | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine Leiomyoma | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 3 / 421 (0.71%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic Dilatation | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive Crisis | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Spontaneous | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 2 / 421 (0.48%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Adverse Drug Reaction | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injection Site Erythema | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic Reaction | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug Hypersensitivity | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eosinophilic Granulomatosis With Polyangiitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |
| Miscarriage Of Partner | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Adenomyosis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign Prostatic Hyperplasia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial Hyperplasia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic Ovarian Cyst | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian Cyst | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|------------------|
| Vaginal Prolapse | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute Respiratory Failure | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 2 / 421 (0.48%) | 13 / 517 (2.51%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasal Septum Deviation | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasal Septum Perforation | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural Effusion | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Pulmonary Embolism | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Oedema | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory Failure | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis Noninfective | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Status Asthmaticus | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal Cord Polyp | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depressed Mood | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide Attempt | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine Aminotransferase Increased | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle Fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chemical Peritonitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Craniocerebral Injury | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Facial Bones Fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Forearm Fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hand Fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Head Injury | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision Site Pain | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional Hernia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower Limb Fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar Vertebral Fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniscus Injury | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post Procedural Complication | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post Procedural Constipation | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Contusion | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radius Fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin Laceration | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper Limb Fracture | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Odontogenic Cyst | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute Coronary Syndrome | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Acute Left Ventricular Failure | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina Unstable | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic Valve Incompetence | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 2 / 421 (0.48%) | 2 / 517 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular Block Complete | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac Failure | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial Ischaemia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Carotid Artery Disease | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral Infarction | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyskinesia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive Cerebrovascular Disease | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Idiopathic Intracranial Hypertension | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuritis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Optic Neuritis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parkinson's Disease | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thalamic Infarction | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Angle Closure Glaucoma | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cataract | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serous Retinal Detachment | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal Hernia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal Incarcerated Hernia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diaphragmatic Hernia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulum Intestinal | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis Erosive | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis Eosinophilic | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiatus Hernia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal Hernia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal Obstruction | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intra-Abdominal Haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large Intestine Polyp | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 2 / 421 (0.48%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal Food Impaction | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retroperitoneum Cyst | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth Impacted | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Umbilical Hernia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper Gastrointestinal Haemorrhage | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis Acute | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatomegaly | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema Nodosum | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash Erythematous | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash Vesicular | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute Kidney Injury | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Iga Nephropathy | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary Incontinence | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 3 / 421 (0.71%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Pain In Extremity | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator Cuff Syndrome | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abscess Limb | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopulmonary Aspergillosis Allergic | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervicitis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Chronic Sinusitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes Simplex Encephalitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large Intestine Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower Respiratory Tract Infection Bacterial | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mycobacterium Avium Complex Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 4 / 421 (0.95%) | 4 / 517 (0.77%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia Bacterial | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post Procedural Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis Acute | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salmonellosis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic Metabolic Decompensation | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Subjects from EFC13579: Dupilumab/Dupilumab | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilumab |
|--|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 106 / 1013 (10.46%) | 12 / 97 (12.37%) | 10 / 90 (11.11%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma Gastric | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma Of Colon | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal Cell Carcinoma | | | |
| subjects affected / exposed | 3 / 1013 (0.30%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign Ovarian Tumour | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bowen's Disease | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast Cancer | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon Adenoma | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon Cancer | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial Cancer | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibroadenoma Of Breast | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Follicular Thyroid Cancer | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric Adenoma | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hodgkin's Disease | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraductal Proliferative Breast Lesion | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Juvenile Melanoma Benign | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large Intestine Benign Neoplasm | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung Cancer Metastatic | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases To Central Nervous System | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-Small Cell Lung Cancer | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteochondroma | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian Cancer | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papillary Thyroid Cancer | | | |
| subjects affected / exposed | 3 / 1013 (0.30%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate Cancer | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate Cancer Stage I | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal Cancer | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous Cell Carcinoma Of Skin | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine Leiomyoma | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Aortic Dilatation | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive Crisis | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Spontaneous | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|------------------|----------------|----------------|
| General disorders and administration site conditions | | | |
| Adverse Drug Reaction | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injection Site Erythema | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic Reaction | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug Hypersensitivity | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eosinophilic Granulomatosis With Polyangiitis | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 1 / 97 (1.03%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |
| Miscarriage Of Partner | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Adenomyosis | | | |

| | | | |
|---|-------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign Prostatic Hyperplasia | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endometrial Hyperplasia | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic Ovarian Cyst | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian Cyst | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vaginal Prolapse | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute Respiratory Failure | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 18 / 1013 (1.78%) | 0 / 97 (0.00%) | 5 / 90 (5.56%) |
| occurrences causally related to treatment / all | 0 / 19 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atelectasis | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasal Septum Deviation | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasal Septum Perforation | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural Effusion | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Embolism | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Oedema | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory Failure | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Sinusitis Noninfective | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Status Asthmaticus | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal Cord Polyp | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depressed Mood | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide Attempt | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine Aminotransferase Increased | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural | | | |

| | | | |
|---|------------------|----------------|----------------|
| complications | | | |
| Ankle Fracture | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chemical Peritonitis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Craniocerebral Injury | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial Bones Fracture | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Forearm Fracture | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hand Fracture | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Head Injury | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision Site Pain | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional Hernia | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower Limb Fracture | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar Vertebral Fracture | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniscus Injury | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post Procedural Complication | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post Procedural Constipation | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Contusion | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radius Fracture | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin Laceration | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper Limb Fracture | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Odontogenic Cyst | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute Coronary Syndrome | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute Left Ventricular Failure | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina Unstable | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic Valve Incompetence | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|----------------|----------------|
| Atrial Fibrillation | | | |
| subjects affected / exposed | 5 / 1013 (0.49%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular Block Complete | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac Failure | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial Ischaemia | | | |
| subjects affected / exposed | 3 / 1013 (0.30%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocarditis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Carotid Artery Disease | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral Infarction | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyskinesia | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive Cerebrovascular Disease | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Idiopathic Intracranial Hypertension | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuritis | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Optic Neuritis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parkinson's Disease | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thalamic Infarction | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Angle Closure Glaucoma | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cataract | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serous Retinal Detachment | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal Hernia | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal Incarcerated Hernia | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diaphragmatic Hernia | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulum Intestinal | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis Erosive | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis Eosinophilic | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiatus Hernia | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal Hernia | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal Obstruction | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intra-Abdominal Haemorrhage | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large Intestine Polyp | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal Food Impaction | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retroperitoneum Cyst | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth Impacted | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Umbilical Hernia | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper Gastrointestinal Haemorrhage | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis Acute | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |
| subjects affected / exposed | 4 / 1013 (0.39%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatomegaly | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema Nodosum | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash Erythematous | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash Vesicular | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute Kidney Injury | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iga Nephropathy | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureterolithiasis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary Incontinence | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |

| | | | |
|---|------------------|----------------|----------------|
| Goitre | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 4 / 1013 (0.39%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain In Extremity | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator Cuff Syndrome | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abscess Limb | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|----------------|----------------|
| Appendicitis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopulmonary Aspergillosis Allergic | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervicitis | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic Sinusitis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear Infection | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes Simplex Encephalitis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large Intestine Infection | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower Respiratory Tract Infection Bacterial | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mycobacterium Avium Complex Infection | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 7 / 1013 (0.69%) | 1 / 97 (1.03%) | 1 / 90 (1.11%) |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia Bacterial | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post Procedural Infection | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis Acute | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salmonellosis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound Infection | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic Metabolic Decompensation | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupilumab | |
|---|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 4 / 14 (28.57%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma Gastric | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma Of Colon | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign Ovarian Tumour | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bowen's Disease | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon Adenoma | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibroadenoma Of Breast | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Follicular Thyroid Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric Adenoma | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hodgkin's Disease | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intraductal Proliferative Breast Lesion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Juvenile Melanoma Benign | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large Intestine Benign Neoplasm | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Cancer Metastatic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases To Central Nervous System | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-Small Cell Lung Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteochondroma | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary Thyroid Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate Cancer Stage I | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal Cancer | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous Cell Carcinoma Of Skin | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine Leiomyoma | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Aortic Dilatation | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive Crisis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Spontaneous | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Adverse Drug Reaction | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injection Site Erythema | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic Reaction | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug Hypersensitivity | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eosinophilic Granulomatosis With Polyangiitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Social circumstances | | | |
| Miscarriage Of Partner | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Adenomyosis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign Prostatic Hyperplasia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial Hyperplasia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|----------------|----------------|--|
| Haemorrhagic Ovarian Cyst | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian Cyst | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal Prolapse | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute Respiratory Failure | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal Septum Deviation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal Septum Perforation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|----------------|----------------|--|
| Pleural Effusion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Embolism | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Oedema | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory Failure | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis Noninfective | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Status Asthmaticus | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vocal Cord Polyp | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |

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|---|----------------|----------------|--|
| Delirium | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depressed Mood | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide Attempt | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine Aminotransferase Increased | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Ankle Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chemical Peritonitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Craniocerebral Injury | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Facial Bones Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Forearm Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head Injury | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incision Site Pain | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incisional Hernia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower Limb Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar Vertebral Fracture | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus Injury | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post Procedural Complication | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post Procedural Constipation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary Contusion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin Laceration | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper Limb Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Odontogenic Cyst | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute Coronary Syndrome | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute Left Ventricular Failure | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina Unstable | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic Valve Incompetence | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular Block Complete | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac Failure | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial Ischaemia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Carotid Artery Disease | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral Infarction | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyskinesia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive Cerebrovascular Disease | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Idiopathic Intracranial Hypertension | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuritis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Optic Neuritis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parkinson's Disease | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thalamic Infarction | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Angle Closure Glaucoma | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Serous Retinal Detachment | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Hernia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal Incarcerated Hernia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diaphragmatic Hernia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum Intestinal | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis Erosive | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis Eosinophilic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus Hernia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal Hernia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal Obstruction | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intra-Abdominal Haemorrhage | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large Intestine Polyp | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal Food Impaction | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retroperitoneum Cyst | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth Impacted | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Umbilical Hernia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper Gastrointestinal Haemorrhage | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis Acute | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatomegaly | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema Nodosum | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash Erythematous | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash Vesicular | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute Kidney Injury | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iga Nephropathy | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary Incontinence | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain In Extremity | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rotator Cuff Syndrome | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess Limb | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopulmonary Aspergillosis Allergic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Cellulitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervicitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic Sinusitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear Infection | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes Simplex Encephalitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large Intestine Infection | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower Respiratory Tract Infection Bacterial | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mycobacterium Avium Complex Infection | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia Bacterial | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post Procedural Infection | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis Acute | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonellosis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound Infection | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic Metabolic Decompensation | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 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 | Subjects from DRI12544: Placebo/Dupilumab | Subjects from DRI12544: Dupilumab/Dupilumab | Subjects from EFC13579: Placebo/Dupilumab |
|--|---|---|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 80 / 111 (72.07%) | 323 / 421 (76.72%) | 357 / 517 (69.05%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Pituitary Tumour Benign subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 0 / 421 (0.00%) 0 | 0 / 517 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 5 / 111 (4.50%) 5 | 16 / 421 (3.80%) 19 | 19 / 517 (3.68%) 20 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 1 / 111 (0.90%) 1 | 10 / 421 (2.38%) 12 | 5 / 517 (0.97%) 5 |
| Injection Site Bruising subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 1 / 421 (0.24%) 2 | 1 / 517 (0.19%) 1 |
| Injection Site Erythema subjects affected / exposed occurrences (all) | 26 / 111 (23.42%) 102 | 55 / 421 (13.06%) 412 | 35 / 517 (6.77%) 148 |
| Injection Site Haematoma subjects affected / exposed occurrences (all) | 4 / 111 (3.60%) 4 | 2 / 421 (0.48%) 2 | 4 / 517 (0.77%) 4 |
| Injection Site Haemorrhage subjects affected / exposed occurrences (all) | 5 / 111 (4.50%) 7 | 5 / 421 (1.19%) 5 | 5 / 517 (0.97%) 5 |
| Injection Site Oedema subjects affected / exposed occurrences (all) | 4 / 111 (3.60%) 9 | 14 / 421 (3.33%) 84 | 14 / 517 (2.71%) 32 |
| Injection Site Pain | | | |

| | | | |
|---|-------------------|------------------|------------------|
| subjects affected / exposed | 9 / 111 (8.11%) | 18 / 421 (4.28%) | 15 / 517 (2.90%) |
| occurrences (all) | 18 | 28 | 40 |
| Injection Site Pruritus | | | |
| subjects affected / exposed | 12 / 111 (10.81%) | 16 / 421 (3.80%) | 15 / 517 (2.90%) |
| occurrences (all) | 23 | 54 | 36 |
| Injection Site Reaction | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 3 / 517 (0.58%) |
| occurrences (all) | 0 | 1 | 3 |
| Injection Site Warmth | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Peripheral Swelling | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 3 / 517 (0.58%) |
| occurrences (all) | 0 | 1 | 3 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 8 / 421 (1.90%) | 0 / 517 (0.00%) |
| occurrences (all) | 1 | 12 | 0 |
| Immune system disorders | | | |
| Drug Hypersensitivity | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences (all) | 1 | 0 | 1 |
| Multiple Allergies | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Endometriosis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metrorrhagia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|------------------------------------|-----------------|------------------|------------------|
| Cough | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 16 / 421 (3.80%) | 10 / 517 (1.93%) |
| occurrences (all) | 4 | 24 | 12 |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 10 / 421 (2.38%) | 8 / 517 (1.55%) |
| occurrences (all) | 2 | 11 | 8 |
| Nasal Congestion | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 5 / 421 (1.19%) | 3 / 517 (0.58%) |
| occurrences (all) | 1 | 5 | 3 |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 13 / 421 (3.09%) | 11 / 517 (2.13%) |
| occurrences (all) | 5 | 13 | 11 |
| Paranasal Sinus Discomfort | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus Congestion | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 2 / 517 (0.39%) |
| occurrences (all) | 0 | 1 | 3 |
| Sputum Increased | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Upper Respiratory Tract Congestion | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 3 / 517 (0.58%) |
| occurrences (all) | 1 | 0 | 5 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 421 (0.24%) | 7 / 517 (1.35%) |
| occurrences (all) | 1 | 1 | 7 |
| Insomnia | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 6 / 421 (1.43%) | 6 / 517 (1.16%) |
| occurrences (all) | 3 | 7 | 6 |
| Sleep Disorder | | | |

| | | | |
|--|----------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 0 / 421 (0.00%) 0 | 1 / 517 (0.19%) 1 |
| Investigations | | | |
| Blood Glucose Increased subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 0 / 421 (0.00%) 0 | 1 / 517 (0.19%) 1 |
| C-Reactive Protein Increased subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 0 / 421 (0.00%) 0 | 0 / 517 (0.00%) 0 |
| Epstein-Barr Virus Test Positive subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 0 / 421 (0.00%) 0 | 0 / 517 (0.00%) 0 |
| White Blood Cells Urine Positive subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 0 / 421 (0.00%) 0 | 0 / 517 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental Overdose subjects affected / exposed occurrences (all) | 6 / 111 (5.41%) 9 | 40 / 421 (9.50%) 44 | 28 / 517 (5.42%) 31 |
| Arthropod Bite subjects affected / exposed occurrences (all) | 2 / 111 (1.80%) 2 | 4 / 421 (0.95%) 5 | 3 / 517 (0.58%) 3 |
| Concussion subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 0 / 421 (0.00%) 0 | 0 / 517 (0.00%) 0 |
| Contusion subjects affected / exposed occurrences (all) | 3 / 111 (2.70%) 3 | 14 / 421 (3.33%) 27 | 12 / 517 (2.32%) 13 |
| Fall subjects affected / exposed occurrences (all) | 2 / 111 (1.80%) 2 | 7 / 421 (1.66%) 8 | 12 / 517 (2.32%) 12 |
| Intentional Overdose subjects affected / exposed occurrences (all) | 1 / 111 (0.90%) 1 | 3 / 421 (0.71%) 3 | 0 / 517 (0.00%) 0 |
| Limb Injury | | | |

| | | | |
|-----------------------------|-------------------|-------------------|------------------|
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 421 (0.24%) | 3 / 517 (0.58%) |
| occurrences (all) | 1 | 2 | 3 |
| Lip Injury | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle Strain | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin Laceration | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 5 / 421 (1.19%) | 10 / 517 (1.93%) |
| occurrences (all) | 1 | 5 | 10 |
| Stab Wound | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth Fracture | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 1 / 421 (0.24%) | 1 / 517 (0.19%) |
| occurrences (all) | 3 | 1 | 1 |
| Wrist Fracture | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 2 / 517 (0.39%) |
| occurrences (all) | 0 | 0 | 2 |
| Nervous system disorders | | | |
| Carpal Tunnel Syndrome | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 12 / 421 (2.85%) | 8 / 517 (1.55%) |
| occurrences (all) | 3 | 13 | 8 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 13 / 111 (11.71%) | 47 / 421 (11.16%) | 47 / 517 (9.09%) |
| occurrences (all) | 14 | 141 | 69 |
| Migraine | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 3 / 421 (0.71%) | 7 / 517 (1.35%) |
| occurrences (all) | 2 | 3 | 14 |

| | | | |
|--|----------------------|------------------------|-----------------------|
| Paraesthesia subjects affected / exposed occurrences (all) | 1 / 111 (0.90%) 1 | 3 / 421 (0.71%) 3 | 1 / 517 (0.19%) 1 |
| Presyncope subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 2 / 421 (0.48%) 2 | 0 / 517 (0.00%) 0 |
| Somnolence subjects affected / exposed occurrences (all) | 1 / 111 (0.90%) 1 | 4 / 421 (0.95%) 6 | 1 / 517 (0.19%) 1 |
| Syncope subjects affected / exposed occurrences (all) | 1 / 111 (0.90%) 1 | 1 / 421 (0.24%) 1 | 0 / 517 (0.00%) 0 |
| Ear and labyrinth disorders Ear Pain subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 2 / 421 (0.48%) 2 | 1 / 517 (0.19%) 1 |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 2 / 421 (0.48%) 2 | 3 / 517 (0.58%) 3 |
| Eye disorders Dry Eye subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 4 / 421 (0.95%) 5 | 2 / 517 (0.39%) 2 |
| Gastrointestinal disorders Abdominal Distension subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 2 / 421 (0.48%) 2 | 1 / 517 (0.19%) 1 |
| Abdominal Pain subjects affected / exposed occurrences (all) | 3 / 111 (2.70%) 3 | 12 / 421 (2.85%) 13 | 9 / 517 (1.74%) 11 |
| Abdominal Pain Upper subjects affected / exposed occurrences (all) | 0 / 111 (0.00%) 0 | 5 / 421 (1.19%) 5 | 6 / 517 (1.16%) 6 |
| Dental Caries subjects affected / exposed occurrences (all) | 1 / 111 (0.90%) 2 | 6 / 421 (1.43%) 6 | 4 / 517 (0.77%) 4 |
| Diarrhoea | | | |

| | | | |
|--|-----------------|------------------|------------------|
| subjects affected / exposed | 3 / 111 (2.70%) | 16 / 421 (3.80%) | 7 / 517 (1.35%) |
| occurrences (all) | 3 | 20 | 9 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 421 (0.24%) | 1 / 517 (0.19%) |
| occurrences (all) | 1 | 2 | 1 |
| Gastrointestinal Disorder | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal Reflux Disease | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 13 / 421 (3.09%) | 13 / 517 (2.51%) |
| occurrences (all) | 1 | 14 | 15 |
| Haemorrhoidal Haemorrhage | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 6 / 421 (1.43%) | 8 / 517 (1.55%) |
| occurrences (all) | 2 | 36 | 8 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 1 / 517 (0.19%) |
| occurrences (all) | 0 | 0 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 4 / 421 (0.95%) | 5 / 517 (0.97%) |
| occurrences (all) | 2 | 4 | 5 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis Atopic | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 2 / 421 (0.48%) | 5 / 517 (0.97%) |
| occurrences (all) | 0 | 5 | 5 |
| Dyshidrotic Eczema | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Papulopustular Rosacea | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pityriasis Alba | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|-----------------|------------------|------------------|
| Rash Generalised | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 421 (0.24%) | 1 / 517 (0.19%) |
| occurrences (all) | 1 | 1 | 1 |
| Rosacea | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 1 / 517 (0.19%) |
| occurrences (all) | 0 | 1 | 1 |
| Solar Dermatitis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Renal and urinary disorders | | | |
| Leukocyturia | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary Retention | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 9 / 111 (8.11%) | 23 / 421 (5.46%) | 23 / 517 (4.45%) |
| occurrences (all) | 10 | 29 | 29 |
| Back Pain | | | |
| subjects affected / exposed | 4 / 111 (3.60%) | 30 / 421 (7.13%) | 23 / 517 (4.45%) |
| occurrences (all) | 4 | 33 | 28 |
| Bursitis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 2 / 421 (0.48%) | 2 / 517 (0.39%) |
| occurrences (all) | 2 | 2 | 2 |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 6 / 421 (1.43%) | 3 / 517 (0.58%) |
| occurrences (all) | 0 | 6 | 3 |
| Muscle Spasms | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 4 / 421 (0.95%) | 7 / 517 (1.35%) |
| occurrences (all) | 2 | 6 | 9 |
| Myalgia | | | |
| subjects affected / exposed | 5 / 111 (4.50%) | 14 / 421 (3.33%) | 7 / 517 (1.35%) |
| occurrences (all) | 5 | 14 | 7 |
| Myositis | | | |

| | | | |
|-----------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 2 / 517 (0.39%) |
| occurrences (all) | 0 | 1 | 2 |
| Pain In Extremity | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 6 / 421 (1.43%) | 7 / 517 (1.35%) |
| occurrences (all) | 2 | 6 | 8 |
| Rotator Cuff Syndrome | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 1 / 421 (0.24%) | 1 / 517 (0.19%) |
| occurrences (all) | 1 | 1 | 1 |
| Tendonitis | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 4 / 421 (0.95%) | 0 / 517 (0.00%) |
| occurrences (all) | 3 | 4 | 0 |
| Trismus | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 15 / 111 (13.51%) | 80 / 421 (19.00%) | 63 / 517 (12.19%) |
| occurrences (all) | 30 | 135 | 100 |
| Bronchitis Viral | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 5 / 421 (1.19%) | 5 / 517 (0.97%) |
| occurrences (all) | 0 | 5 | 5 |
| Gastroenteritis | | | |
| subjects affected / exposed | 6 / 111 (5.41%) | 7 / 421 (1.66%) | 10 / 517 (1.93%) |
| occurrences (all) | 6 | 8 | 14 |
| Genital Herpes | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 3 / 421 (0.71%) | 0 / 517 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------------|-------------------|--------------------|-------------------|
| Influenza | | | |
| subjects affected / exposed | 5 / 111 (4.50%) | 44 / 421 (10.45%) | 30 / 517 (5.80%) |
| occurrences (all) | 5 | 52 | 39 |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 6 / 421 (1.43%) | 6 / 517 (1.16%) |
| occurrences (all) | 2 | 6 | 7 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 27 / 111 (24.32%) | 109 / 421 (25.89%) | 99 / 517 (19.15%) |
| occurrences (all) | 47 | 208 | 149 |
| Oral Candidiasis | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 9 / 421 (2.14%) | 6 / 517 (1.16%) |
| occurrences (all) | 5 | 19 | 9 |
| Pharyngitis | | | |
| subjects affected / exposed | 16 / 111 (14.41%) | 37 / 421 (8.79%) | 26 / 517 (5.03%) |
| occurrences (all) | 21 | 57 | 30 |
| Pharyngitis Streptococcal | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 6 / 517 (1.16%) |
| occurrences (all) | 0 | 2 | 6 |
| Post Procedural Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Postoperative Wound Infection | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 0 / 421 (0.00%) | 0 / 517 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulpitis Dental | | | |
| subjects affected / exposed | 1 / 111 (0.90%) | 2 / 421 (0.48%) | 0 / 517 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Respiratory Tract Infection | | | |
| subjects affected / exposed | 3 / 111 (2.70%) | 15 / 421 (3.56%) | 5 / 517 (0.97%) |
| occurrences (all) | 3 | 17 | 6 |
| Respiratory Tract Infection Viral | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 3 / 421 (0.71%) | 6 / 517 (1.16%) |
| occurrences (all) | 0 | 6 | 7 |
| Rhinitis | | | |
| subjects affected / exposed | 7 / 111 (6.31%) | 11 / 421 (2.61%) | 6 / 517 (1.16%) |
| occurrences (all) | 8 | 11 | 7 |

| | | | |
|---|-------------------|-------------------|-------------------|
| Sinusitis | | | |
| subjects affected / exposed | 9 / 111 (8.11%) | 33 / 421 (7.84%) | 32 / 517 (6.19%) |
| occurrences (all) | 16 | 56 | 43 |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 18 / 111 (16.22%) | 60 / 421 (14.25%) | 65 / 517 (12.57%) |
| occurrences (all) | 30 | 87 | 96 |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 5 / 111 (4.50%) | 26 / 421 (6.18%) | 17 / 517 (3.29%) |
| occurrences (all) | 7 | 31 | 20 |
| Viral Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 2 / 111 (1.80%) | 11 / 421 (2.61%) | 13 / 517 (2.51%) |
| occurrences (all) | 3 | 15 | 16 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 111 (0.00%) | 1 / 421 (0.24%) | 1 / 517 (0.19%) |
| occurrences (all) | 0 | 1 | 1 |

| Non-serious adverse events | Subjects from EFC13579: Dupilumab/Dupilum ab | Subjects from EFC13691: Placebo/Dupilumab | Subjects from EFC13691: Dupilumab/Dupilum ab |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 666 / 1013 (65.75%) | 56 / 97 (57.73%) | 55 / 90 (61.11%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Pituitary Tumour Benign | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 29 / 1013 (2.86%) | 5 / 97 (5.15%) | 2 / 90 (2.22%) |
| occurrences (all) | 37 | 7 | 2 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 8 / 1013 (0.79%) | 5 / 97 (5.15%) | 1 / 90 (1.11%) |
| occurrences (all) | 15 | 5 | 1 |
| Injection Site Bruising | | | |

| | | | |
|-----------------------------|-------------------|----------------|----------------|
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Injection Site Erythema | | | |
| subjects affected / exposed | 50 / 1013 (4.94%) | 5 / 97 (5.15%) | 2 / 90 (2.22%) |
| occurrences (all) | 295 | 12 | 29 |
| Injection Site Haematoma | | | |
| subjects affected / exposed | 4 / 1013 (0.39%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 7 | 3 | 0 |
| Injection Site Haemorrhage | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Injection Site Oedema | | | |
| subjects affected / exposed | 15 / 1013 (1.48%) | 0 / 97 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 58 | 0 | 8 |
| Injection Site Pain | | | |
| subjects affected / exposed | 14 / 1013 (1.38%) | 0 / 97 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 51 | 0 | 9 |
| Injection Site Pruritus | | | |
| subjects affected / exposed | 7 / 1013 (0.69%) | 2 / 97 (2.06%) | 0 / 90 (0.00%) |
| occurrences (all) | 20 | 2 | 0 |
| Injection Site Reaction | | | |
| subjects affected / exposed | 5 / 1013 (0.49%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Injection Site Warmth | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 20 | 1 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral Swelling | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 16 / 1013 (1.58%) | 1 / 97 (1.03%) | 3 / 90 (3.33%) |
| occurrences (all) | 20 | 1 | 4 |
| Immune system disorders | | | |

| | | | |
|--|-------------------------|---------------------|---------------------|
| Drug Hypersensitivity subjects affected / exposed occurrences (all) | 4 / 1013 (0.39%) 4 | 2 / 97 (2.06%) 2 | 0 / 90 (0.00%) 0 |
| Multiple Allergies subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Reproductive system and breast disorders | | | |
| Endometriosis subjects affected / exposed occurrences (all) | 1 / 1013 (0.10%) 1 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Metrorrhagia subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 1 / 90 (1.11%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 22 / 1013 (2.17%) 29 | 3 / 97 (3.09%) 3 | 3 / 90 (3.33%) 4 |
| Dyspnoea subjects affected / exposed occurrences (all) | 12 / 1013 (1.18%) 23 | 2 / 97 (2.06%) 7 | 2 / 90 (2.22%) 3 |
| Nasal Congestion subjects affected / exposed occurrences (all) | 5 / 1013 (0.49%) 5 | 0 / 97 (0.00%) 0 | 1 / 90 (1.11%) 1 |
| Oropharyngeal Pain subjects affected / exposed occurrences (all) | 20 / 1013 (1.97%) 22 | 2 / 97 (2.06%) 2 | 5 / 90 (5.56%) 5 |
| Paranasal Sinus Discomfort subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Sinus Congestion subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 1 / 90 (1.11%) 1 |
| Sputum Increased subjects affected / exposed occurrences (all) | 1 / 1013 (0.10%) 1 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Upper Respiratory Tract Congestion | | | |

| | | | |
|--|-------------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Wheezing subjects affected / exposed occurrences (all) | 3 / 1013 (0.30%) 4 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 10 / 1013 (0.99%) 11 | 1 / 97 (1.03%) 1 | 0 / 90 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 8 / 1013 (0.79%) 8 | 1 / 97 (1.03%) 1 | 0 / 90 (0.00%) 0 |
| Sleep Disorder subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Investigations | | | |
| Blood Glucose Increased subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 1 / 90 (1.11%) 1 |
| C-Reactive Protein Increased subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Epstein-Barr Virus Test Positive subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| White Blood Cells Urine Positive subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental Overdose subjects affected / exposed occurrences (all) | 45 / 1013 (4.44%) 48 | 5 / 97 (5.15%) 5 | 5 / 90 (5.56%) 6 |
| Arthropod Bite subjects affected / exposed occurrences (all) | 9 / 1013 (0.89%) 9 | 0 / 97 (0.00%) 0 | 1 / 90 (1.11%) 1 |
| Concussion | | | |

| | | | |
|-----------------------------|-------------------|----------------|----------------|
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 14 / 1013 (1.38%) | 0 / 97 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 18 | 0 | 3 |
| Fall | | | |
| subjects affected / exposed | 33 / 1013 (3.26%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 38 | 1 | 0 |
| Intentional Overdose | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 2 / 97 (2.06%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Limb Injury | | | |
| subjects affected / exposed | 3 / 1013 (0.30%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences (all) | 4 | 0 | 1 |
| Lip Injury | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle Strain | | | |
| subjects affected / exposed | 7 / 1013 (0.69%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Skin Laceration | | | |
| subjects affected / exposed | 7 / 1013 (0.69%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences (all) | 7 | 0 | 1 |
| Stab Wound | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth Fracture | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Wrist Fracture | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Carpal Tunnel Syndrome | | | |
| subjects affected / exposed | 3 / 1013 (0.30%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |

| | | | |
|-----------------------------|-------------------|----------------|----------------|
| Dizziness | | | |
| subjects affected / exposed | 6 / 1013 (0.59%) | 2 / 97 (2.06%) | 0 / 90 (0.00%) |
| occurrences (all) | 7 | 2 | 0 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 74 / 1013 (7.31%) | 4 / 97 (4.12%) | 5 / 90 (5.56%) |
| occurrences (all) | 145 | 4 | 5 |
| Migraine | | | |
| subjects affected / exposed | 9 / 1013 (0.89%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 4 / 1013 (0.39%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 2 / 97 (2.06%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Syncope | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences (all) | 2 | 0 | 3 |
| Ear and labyrinth disorders | | | |
| Ear Pain | | | |
| subjects affected / exposed | 6 / 1013 (0.59%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Eye disorders | | | |
| Dry Eye | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |

| | | | |
|----------------------------------|-------------------|----------------|----------------|
| Abdominal Distension | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal Pain | | | |
| subjects affected / exposed | 13 / 1013 (1.28%) | 4 / 97 (4.12%) | 1 / 90 (1.11%) |
| occurrences (all) | 16 | 4 | 1 |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 10 / 1013 (0.99%) | 1 / 97 (1.03%) | 1 / 90 (1.11%) |
| occurrences (all) | 11 | 1 | 1 |
| Dental Caries | | | |
| subjects affected / exposed | 9 / 1013 (0.89%) | 1 / 97 (1.03%) | 1 / 90 (1.11%) |
| occurrences (all) | 9 | 1 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 25 / 1013 (2.47%) | 4 / 97 (4.12%) | 3 / 90 (3.33%) |
| occurrences (all) | 27 | 4 | 3 |
| Dyspepsia | | | |
| subjects affected / exposed | 7 / 1013 (0.69%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 8 | 1 | 0 |
| Gastrointestinal Disorder | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Gastrooesophageal Reflux Disease | | | |
| subjects affected / exposed | 21 / 1013 (2.07%) | 2 / 97 (2.06%) | 0 / 90 (0.00%) |
| occurrences (all) | 23 | 2 | 0 |
| Haemorrhoidal Haemorrhage | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 14 / 1013 (1.38%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 52 | 0 | 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 13 / 1013 (1.28%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 15 | 0 | 0 |

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|---|-------------------|----------------|----------------|
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis Atopic | | | |
| subjects affected / exposed | 9 / 1013 (0.89%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 11 | 1 | 0 |
| Dyshidrotic Eczema | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Papulopustular Rosacea | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pityriasis Alba | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash Generalised | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rosacea | | | |
| subjects affected / exposed | 3 / 1013 (0.30%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Solar Dermatitis | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal and urinary disorders | | | |
| Leukocyturia | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary Retention | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 22 / 1013 (2.17%) | 7 / 97 (7.22%) | 1 / 90 (1.11%) |
| occurrences (all) | 22 | 7 | 1 |
| Back Pain | | | |
| subjects affected / exposed | 52 / 1013 (5.13%) | 5 / 97 (5.15%) | 0 / 90 (0.00%) |
| occurrences (all) | 67 | 5 | 0 |

| | | | |
|--------------------------------|---------------------|----------------|------------------|
| Bursitis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 3 / 1013 (0.30%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Muscle Spasms | | | |
| subjects affected / exposed | 9 / 1013 (0.89%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 12 / 1013 (1.18%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences (all) | 14 | 0 | 1 |
| Myositis | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pain In Extremity | | | |
| subjects affected / exposed | 16 / 1013 (1.58%) | 1 / 97 (1.03%) | 3 / 90 (3.33%) |
| occurrences (all) | 16 | 1 | 3 |
| Rotator Cuff Syndrome | | | |
| subjects affected / exposed | 2 / 1013 (0.20%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tendonitis | | | |
| subjects affected / exposed | 5 / 1013 (0.49%) | 1 / 97 (1.03%) | 2 / 90 (2.22%) |
| occurrences (all) | 5 | 1 | 2 |
| Trismus | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 117 / 1013 (11.55%) | 9 / 97 (9.28%) | 14 / 90 (15.56%) |
| occurrences (all) | 181 | 10 | 15 |
| Bronchitis Viral | | | |
| subjects affected / exposed | 4 / 1013 (0.39%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Conjunctivitis | | | |

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| subjects affected / exposed | 18 / 1013 (1.78%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 21 | 1 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 26 / 1013 (2.57%) | 0 / 97 (0.00%) | 2 / 90 (2.22%) |
| occurrences (all) | 31 | 0 | 2 |
| Genital Herpes | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 1013 (0.10%) | 0 / 97 (0.00%) | 1 / 90 (1.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Infection | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 67 / 1013 (6.61%) | 9 / 97 (9.28%) | 7 / 90 (7.78%) |
| occurrences (all) | 79 | 11 | 10 |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 17 / 1013 (1.68%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 18 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 191 / 1013 (18.85%) | 17 / 97 (17.53%) | 16 / 90 (17.78%) |
| occurrences (all) | 293 | 30 | 22 |
| Oral Candidiasis | | | |
| subjects affected / exposed | 14 / 1013 (1.38%) | 1 / 97 (1.03%) | 0 / 90 (0.00%) |
| occurrences (all) | 19 | 1 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 59 / 1013 (5.82%) | 1 / 97 (1.03%) | 4 / 90 (4.44%) |
| occurrences (all) | 75 | 1 | 5 |
| Pharyngitis Streptococcal | | | |
| subjects affected / exposed | 7 / 1013 (0.69%) | 1 / 97 (1.03%) | 1 / 90 (1.11%) |
| occurrences (all) | 7 | 1 | 1 |
| Post Procedural Infection | | | |
| subjects affected / exposed | 0 / 1013 (0.00%) | 0 / 97 (0.00%) | 0 / 90 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|-------------------------------|----------------------|----------------------|
| Postoperative Wound Infection subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Pulpitis Dental subjects affected / exposed occurrences (all) | 5 / 1013 (0.49%) 6 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Respiratory Tract Infection subjects affected / exposed occurrences (all) | 18 / 1013 (1.78%) 25 | 0 / 97 (0.00%) 0 | 2 / 90 (2.22%) 2 |
| Respiratory Tract Infection Viral subjects affected / exposed occurrences (all) | 11 / 1013 (1.09%) 15 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |
| Rhinitis subjects affected / exposed occurrences (all) | 22 / 1013 (2.17%) 25 | 4 / 97 (4.12%) 4 | 1 / 90 (1.11%) 1 |
| Sinusitis subjects affected / exposed occurrences (all) | 50 / 1013 (4.94%) 66 | 2 / 97 (2.06%) 2 | 4 / 90 (4.44%) 4 |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 130 / 1013 (12.83%) 213 | 8 / 97 (8.25%) 12 | 6 / 90 (6.67%) 15 |
| Urinary Tract Infection subjects affected / exposed occurrences (all) | 42 / 1013 (4.15%) 53 | 4 / 97 (4.12%) 4 | 3 / 90 (3.33%) 3 |
| Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 30 / 1013 (2.96%) 48 | 1 / 97 (1.03%) 4 | 1 / 90 (1.11%) 3 |
| Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all) | 0 / 1013 (0.00%) 0 | 0 / 97 (0.00%) 0 | 0 / 90 (0.00%) 0 |

| Non-serious adverse events | Subjects from PDY14192: Placebo/Dupilumab | Subjects from PDY14192: Dupilumab/Dupiluma b | |
|---|---|---|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 18 / 19 (94.74%) | 13 / 14 (92.86%) | |

| | | | |
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| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Pituitary Tumour Benign subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 0 / 14 (0.00%) 0 | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Injection Site Bruising subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Injection Site Erythema subjects affected / exposed occurrences (all) | 8 / 19 (42.11%) 21 | 6 / 14 (42.86%) 29 | |
| Injection Site Haematoma subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 2 / 14 (14.29%) 2 | |
| Injection Site Haemorrhage subjects affected / exposed occurrences (all) | 2 / 19 (10.53%) 2 | 0 / 14 (0.00%) 0 | |
| Injection Site Oedema subjects affected / exposed occurrences (all) | 3 / 19 (15.79%) 6 | 2 / 14 (14.29%) 4 | |
| Injection Site Pain subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 3 | 2 / 14 (14.29%) 2 | |
| Injection Site Pruritus subjects affected / exposed occurrences (all) | 2 / 19 (10.53%) 3 | 0 / 14 (0.00%) 0 | |
| Injection Site Reaction subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |

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| Injection Site Warmth subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Malaise subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Peripheral Swelling subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Immune system disorders Drug Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Multiple Allergies subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Reproductive system and breast disorders Endometriosis subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Metrorrhagia subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 3 / 19 (15.79%) 3 | 0 / 14 (0.00%) 0 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 2 / 19 (10.53%) 2 | 1 / 14 (7.14%) 1 | |
| Nasal Congestion subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |

| | | | |
|---|----------------------|---------------------|--|
| Oropharyngeal Pain subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 1 / 14 (7.14%) 1 | |
| Paranasal Sinus Discomfort subjects affected / exposed occurrences (all) | 2 / 19 (10.53%) 2 | 0 / 14 (0.00%) 0 | |
| Sinus Congestion subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Sputum Increased subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Upper Respiratory Tract Congestion subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Wheezing subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Sleep Disorder subjects affected / exposed occurrences (all) | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 | |
| Investigations Blood Glucose Increased subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| C-Reactive Protein Increased subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Epstein-Barr Virus Test Positive | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| White Blood Cells Urine Positive | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 2 | |
| Injury, poisoning and procedural complications | | | |
| Accidental Overdose | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Arthropod Bite | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Concussion | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Contusion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 3 / 14 (21.43%) | |
| occurrences (all) | 0 | 3 | |
| Fall | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Intentional Overdose | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Limb Injury | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 2 / 14 (14.29%) | |
| occurrences (all) | 0 | 2 | |
| Lip Injury | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Muscle Strain | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Skin Laceration | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Stab Wound | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tooth Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Wrist Fracture | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Carpal Tunnel Syndrome | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 14 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Dysaesthesia | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Headache | | | |
| subjects affected / exposed | 4 / 19 (21.05%) | 1 / 14 (7.14%) | |
| occurrences (all) | 9 | 1 | |
| Migraine | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 2 / 14 (14.29%) | |
| occurrences (all) | 0 | 2 | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|--|--|--|--|
| Syncope subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Ear and labyrinth disorders Ear Pain subjects affected / exposed occurrences (all) Tinnitus subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 0 / 19 (0.00%) 0 | 0 / 14 (0.00%) 0 1 / 14 (7.14%) 1 | |
| Eye disorders Dry Eye subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Gastrointestinal disorders Abdominal Distension subjects affected / exposed occurrences (all) Abdominal Pain subjects affected / exposed occurrences (all) Abdominal Pain Upper subjects affected / exposed occurrences (all) Dental Caries subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Gastrointestinal Disorder subjects affected / exposed occurrences (all) Gastrooesophageal Reflux Disease | 1 / 19 (5.26%) 1 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 1 / 19 (5.26%) 1 2 / 19 (10.53%) 2 0 / 19 (0.00%) 0 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 2 / 14 (14.29%) 2 1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 | |

| | | | |
|--|-----------------|----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Haemorrhoidal Haemorrhage | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 19 (15.79%) | 1 / 14 (7.14%) | |
| occurrences (all) | 4 | 1 | |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 19 (21.05%) | 0 / 14 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis Atopic | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Dyshidrotic Eczema | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Papulopustular Rosacea | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Pityriasis Alba | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Rash Generalised | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rosacea | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Solar Dermatitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|-----------------|-----------------|--|
| Renal and urinary disorders | | | |
| Leukocyturia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Urinary Retention | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 2 / 14 (14.29%) | |
| occurrences (all) | 0 | 2 | |
| Back Pain | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 3 / 14 (21.43%) | |
| occurrences (all) | 2 | 4 | |
| Bursitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Intervertebral Disc Protrusion | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Muscle Spasms | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Myalgia | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Myositis | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain In Extremity | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Rotator Cuff Syndrome | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Tendonitis | | | |

| | | | |
|-----------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Trismus | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Bronchitis Viral | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Genital Herpes | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Infection | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Influenza | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 2 / 14 (14.29%) | |
| occurrences (all) | 2 | 2 | |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 19 (15.79%) | 6 / 14 (42.86%) | |
| occurrences (all) | 8 | 8 | |

| | | |
|-----------------------------------|-----------------|----------------|
| Oral Candidiasis | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pharyngitis | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 0 |
| Pharyngitis Streptococcal | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 |
| Post Procedural Infection | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 |
| Postoperative Wound Infection | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 |
| Pulpitis Dental | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 |
| Respiratory Tract Infection | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 |
| Respiratory Tract Infection Viral | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rhinitis | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 |
| Sinusitis | | |
| subjects affected / exposed | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 |
| Upper Respiratory Tract Infection | | |
| subjects affected / exposed | 2 / 19 (10.53%) | 0 / 14 (0.00%) |
| occurrences (all) | 4 | 0 |
| Urinary Tract Infection | | |
| subjects affected / exposed | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 |

| | | | |
|---|---------------------|---------------------|--|
| Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |
| Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all) | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 04 June 2015 | Following amendment were done: opened eligibility for study entry to United States subjects in the DRI12544 study, as well as to eligible subjects from PDY14192, EFC13579, and EFC13691 studies; changes to inclusion/ exclusion criteria; changes to IMP formulation: as the prefilled syringes became available, subjects were switched to prefilled syringes instead of the vial packaging. |
| 31 October 2016 | Following amendment were done: amended the open-label treatment duration to 48 weeks (1 year); shortened the 16-week post-treatment period to 12 weeks; simplified the study procedures; harmonised protocol exclusion criteria with asthma parent study protocols. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported