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)	EMEA-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.

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Investigational medicinal product name	Dupilumab
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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/Dupilumab	
Number of subjects	19	14	2282
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	41.8	44.9	
standard deviation	± 10.6	± 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
AnyTEAE 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
AnyTEAE led to permanent treatment discontinuation	4	5	1	2

Statistical analyses

No statistical analyses for this end point

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 (≤) 95 millimetres of mercury (mmHg) and decrease from baseline (DFB) greater than or equal to (≥) 20 mmHg; ≥ 160 mmHg and increase from baseline (IFB) ≥ 20 mmHg
•Diastolic blood pressure (DBP): ≤ 45 mmHg and DFB ≥ 10 mmHg; ≥ 110 mmHg and IFB ≥ 10 mmHg
•Heart rate (HR): ≤ 50 beats per minute (bpm) and DFB ≥20 bpm; ≥120 bpm and IFB ≥20 bpm
•Respiratory rate (RR): less than (<) 12 breaths/min(b/m); greater than (>) 20 b/m
•Weight (Wt.) (kg): ≥5 percent (%) DFB; ≥ 5% IFB
•Temperature (T): ≥ 38.0 degree Celsius (°C) rectal/ear/temporal; ≥37.5°C oral; ≥ 37.2°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:≤95&DFB≥20mmHg(n=111,421,516,1013,97,90,19,14)	4	12	19	40
SBP≥160&IFB≥20mmHg(n=111,421,516,1013,97,90,19,14)	2	17	21	45
DBP:≤45&DFB≥10mmHg(n=111,421,516,1013,97,90,19,14)	1	1	11	15
DBP≥110&IFB≥10mmHg(n=111,421,516,1013,97,90,19,14)	0	4	15	20
HR:≤50&DFB ≥20bpm(n=111,421,516,1013,97,90,19	0	3	2	12
HR:≥120&IFB ≥20bpm(n=111,421,516,1013,97,90,19	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.:≥5% DFB (n=111,421,516,1013,97,90,19,14)	32	106	146	261
Wt.≥5% IFB(n=111,421,485,958;96,89,19,14)	45	181	189	378
T:≥38.0°C(n=111,421,516,1013,97,90,19,14)	0	0	1	1
T:≥37.5°C(n=111,421,516,1013,97,90,19,14)	1	0	9	6
T:≥37.2°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	0	0	0	0
HR:≥120&IFB ≥20bpm(n=111,421,516,1013,97,90,19	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:≥700G/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 (± 76.71)	22.95 (± 70.06)		
Week 96 (n=92,340)	13.63 (± 83.88)	21.69 (± 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 (± 75.00)	11.97 (± 72.19)		
Week 96 (n=89,327)	1.16 (± 79.47)	10.05 (± 79.47)		

Statistical analyses

No statistical analyses for this end point

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 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/Dupilumab	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	

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	

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			

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	0 / 111 (0.00%)	0 / 421 (0.00%)	0 / 517 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 111 (4.50%)	16 / 421 (3.80%)	19 / 517 (3.68%)
occurrences (all)	5	19	20
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 111 (0.90%)	10 / 421 (2.38%)	5 / 517 (0.97%)
occurrences (all)	1	12	5
Injection Site Bruising			
subjects affected / exposed	0 / 111 (0.00%)	1 / 421 (0.24%)	1 / 517 (0.19%)
occurrences (all)	0	2	1
Injection Site Erythema			
subjects affected / exposed	26 / 111 (23.42%)	55 / 421 (13.06%)	35 / 517 (6.77%)
occurrences (all)	102	412	148
Injection Site Haematoma			
subjects affected / exposed	4 / 111 (3.60%)	2 / 421 (0.48%)	4 / 517 (0.77%)
occurrences (all)	4	2	4
Injection Site Haemorrhage			
subjects affected / exposed	5 / 111 (4.50%)	5 / 421 (1.19%)	5 / 517 (0.97%)
occurrences (all)	7	5	5
Injection Site Oedema			
subjects affected / exposed	4 / 111 (3.60%)	14 / 421 (3.33%)	14 / 517 (2.71%)
occurrences (all)	9	84	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	0 / 111 (0.00%)	0 / 421 (0.00%)	1 / 517 (0.19%)
occurrences (all)	0	0	1
Investigations			
Blood Glucose Increased			
subjects affected / exposed	0 / 111 (0.00%)	0 / 421 (0.00%)	1 / 517 (0.19%)
occurrences (all)	0	0	1
C-Reactive Protein Increased			
subjects affected / exposed	0 / 111 (0.00%)	0 / 421 (0.00%)	0 / 517 (0.00%)
occurrences (all)	0	0	0
Epstein-Barr Virus Test Positive			
subjects affected / exposed	0 / 111 (0.00%)	0 / 421 (0.00%)	0 / 517 (0.00%)
occurrences (all)	0	0	0
White Blood Cells Urine Positive			
subjects affected / exposed	0 / 111 (0.00%)	0 / 421 (0.00%)	0 / 517 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental Overdose			
subjects affected / exposed	6 / 111 (5.41%)	40 / 421 (9.50%)	28 / 517 (5.42%)
occurrences (all)	9	44	31
Arthropod Bite			
subjects affected / exposed	2 / 111 (1.80%)	4 / 421 (0.95%)	3 / 517 (0.58%)
occurrences (all)	2	5	3
Concussion			
subjects affected / exposed	0 / 111 (0.00%)	0 / 421 (0.00%)	0 / 517 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	3 / 111 (2.70%)	14 / 421 (3.33%)	12 / 517 (2.32%)
occurrences (all)	3	27	13
Fall			
subjects affected / exposed	2 / 111 (1.80%)	7 / 421 (1.66%)	12 / 517 (2.32%)
occurrences (all)	2	8	12
Intentional Overdose			
subjects affected / exposed	1 / 111 (0.90%)	3 / 421 (0.71%)	0 / 517 (0.00%)
occurrences (all)	1	3	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	1 / 111 (0.90%)	3 / 421 (0.71%)	1 / 517 (0.19%)
occurrences (all)	1	3	1
Presyncope			
subjects affected / exposed	0 / 111 (0.00%)	2 / 421 (0.48%)	0 / 517 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	1 / 111 (0.90%)	4 / 421 (0.95%)	1 / 517 (0.19%)
occurrences (all)	1	6	1
Syncope			
subjects affected / exposed	1 / 111 (0.90%)	1 / 421 (0.24%)	0 / 517 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	0 / 111 (0.00%)	2 / 421 (0.48%)	1 / 517 (0.19%)
occurrences (all)	0	2	1
Tinnitus			
subjects affected / exposed	0 / 111 (0.00%)	2 / 421 (0.48%)	3 / 517 (0.58%)
occurrences (all)	0	2	3
Eye disorders			
Dry Eye			
subjects affected / exposed	0 / 111 (0.00%)	4 / 421 (0.95%)	2 / 517 (0.39%)
occurrences (all)	0	5	2
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 111 (0.00%)	2 / 421 (0.48%)	1 / 517 (0.19%)
occurrences (all)	0	2	1
Abdominal Pain			
subjects affected / exposed	3 / 111 (2.70%)	12 / 421 (2.85%)	9 / 517 (1.74%)
occurrences (all)	3	13	11
Abdominal Pain Upper			
subjects affected / exposed	0 / 111 (0.00%)	5 / 421 (1.19%)	6 / 517 (1.16%)
occurrences (all)	0	5	6
Dental Caries			
subjects affected / exposed	1 / 111 (0.90%)	6 / 421 (1.43%)	4 / 517 (0.77%)
occurrences (all)	2	6	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/Dupilumab	Subjects from EFC13691: Placebo/Dupilumab	Subjects from EFC13691: Dupilumab/Dupilumab
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	4 / 1013 (0.39%)	2 / 97 (2.06%)	0 / 90 (0.00%)
occurrences (all)	4	2	0
Multiple Allergies			
subjects affected / exposed	0 / 1013 (0.00%)	0 / 97 (0.00%)	0 / 90 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Endometriosis			
subjects affected / exposed	1 / 1013 (0.10%)	0 / 97 (0.00%)	0 / 90 (0.00%)
occurrences (all)	1	0	0
Metrorrhagia			
subjects affected / exposed	0 / 1013 (0.00%)	0 / 97 (0.00%)	1 / 90 (1.11%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	22 / 1013 (2.17%)	3 / 97 (3.09%)	3 / 90 (3.33%)
occurrences (all)	29	3	4
Dyspnoea			
subjects affected / exposed	12 / 1013 (1.18%)	2 / 97 (2.06%)	2 / 90 (2.22%)
occurrences (all)	23	7	3
Nasal Congestion			
subjects affected / exposed	5 / 1013 (0.49%)	0 / 97 (0.00%)	1 / 90 (1.11%)
occurrences (all)	5	0	1
Oropharyngeal Pain			
subjects affected / exposed	20 / 1013 (1.97%)	2 / 97 (2.06%)	5 / 90 (5.56%)
occurrences (all)	22	2	5
Paranasal Sinus Discomfort			
subjects affected / exposed	0 / 1013 (0.00%)	0 / 97 (0.00%)	0 / 90 (0.00%)
occurrences (all)	0	0	0
Sinus Congestion			
subjects affected / exposed	0 / 1013 (0.00%)	0 / 97 (0.00%)	1 / 90 (1.11%)
occurrences (all)	0	0	1
Sputum Increased			
subjects affected / exposed	1 / 1013 (0.10%)	0 / 97 (0.00%)	0 / 90 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Congestion			

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

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			

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

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

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

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

Oropharyngeal Pain			
subjects affected / exposed	1 / 19 (5.26%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Paranasal Sinus Discomfort			
subjects affected / exposed	2 / 19 (10.53%)	0 / 14 (0.00%)	
occurrences (all)	2	0	
Sinus Congestion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Sputum Increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Upper Respiratory Tract Congestion			
subjects affected / exposed	0 / 19 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 19 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Sleep Disorder			
subjects affected / exposed	0 / 19 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Investigations			
Blood Glucose Increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
C-Reactive Protein Increased			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	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	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear Pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	0 / 19 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Eye disorders			
Dry Eye			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Abdominal Pain			
subjects affected / exposed	0 / 19 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Abdominal Pain Upper			
subjects affected / exposed	0 / 19 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Dental Caries			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	2 / 19 (10.53%)	2 / 14 (14.29%)	
occurrences (all)	2	2	
Dyspepsia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Gastrointestinal Disorder			
subjects affected / exposed	1 / 19 (5.26%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal Reflux Disease			

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