Clinical trial results:
A Multinational, Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study Followed by an Active Treatment Period, to Evaluate the Efficacy, Safety, and Tolerability of Two Doses of Oral Administration of Laquinimod (0.6 mg/day or 1.2 mg/day) in Patients with Relapsing Remitting Multiple Sclerosis

Summary

EudraCT number	2012-003647-30
Trial protocol	BE GB LV DE HU ES GR EE CZ IT AT PL BG SK
Global end of trial date	04 July 2017

Results information

Result version number	v1 (current)
This version publication date	08 March 2019
First version publication date	08 March 2019

Trial information

Trial identification

Sponsor protocol code	LAQ-MS-305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01707992
WHO universal trial number (UTN)	-
Other trial identifiers	Study Name: CONCERTO

Notes:

Sponsors

Sponsor organisation name	Teva Pharmaceutical Industries Ltd
Sponsor organisation address	5 Basel Street, Petach Tiqva, Israel, 49131
Public contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., +01 215-591-3000, info.era-clinical@teva.de
Scientific contact	Director, Clinical Research, Teva Branded Pharmaceutical Products, R&D Inc., +01 215-591-3000, info.era-clinical@teva.de

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 July 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy, safety, and tolerability of a daily dose of 0.6 and 1.2 milligrams (mg) of laquinimod as compared to placebo in participants with relapsing-remitting multiple sclerosis (RRMS).

Protection of trial subjects:

This study was conducted in full accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations (example, Code of Federal Regulations Title 21, Parts 50, 54, 56, 312, and 314; European Union Directive 2001/20/EC on the approximation of the laws, regulations, and administrative provisions of the Member States relating to the implementation of GCP in the conduct of clinical studies on medicinal products for human use). The investigator at each study site was responsible for the conduct and administration of the study at that site and for contacts with study site management, with the Independent Ethics Committee (IEC)/Institutional Review Board (IRB), and with local authorities. Written and/or oral information about the study was provided to all participants in a language understandable by the participants. The information included an adequate explanation of the aims, methods, anticipated benefits, potential hazards, and insurance arrangements in force. Written informed consent was obtained from each participants before any study procedures or assessments were done. It was explained to the participants that they were free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment. Each participant's willingness to participate in the study was documented in writing in a consent form that was signed by the participants with the date of that signature indicated.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 February 2013
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	United States: 44
Country: Number of subjects enrolled	Czech Republic: 42
Country: Number of subjects enrolled	Germany: 38
Country: Number of subjects enrolled	Moldova, Republic of: 36
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	France: 28
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	Austria: 26
Country: Number of subjects enrolled	Estonia: 25
Country: Number of subjects enrolled	Montenegro: 24
Country: Number of subjects enrolled	Croatia: 18

Country: Number of subjects enrolled	Greece: 13
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Latvia: 11
Country: Number of subjects enrolled	Israel: 10
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Slovakia: 3
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Macedonia, the former Yugoslav Republic of: 50
Country: Number of subjects enrolled	Russian Federation: 447
Country: Number of subjects enrolled	Ukraine: 411
Country: Number of subjects enrolled	Bulgaria: 205
Country: Number of subjects enrolled	Poland: 164
Country: Number of subjects enrolled	Romania: 137
Country: Number of subjects enrolled	Belarus: 111
Country: Number of subjects enrolled	Georgia: 106
Country: Number of subjects enrolled	Serbia: 98
Country: Number of subjects enrolled	Bosnia and Herzegovina: 68
Worldwide total number of subjects	2199
EEA total number of subjects	787

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2199
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted at 215 sites in 29 countries.

Period 1

Period 1 title	Placebo-Controlled Phase (24 Months)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo-Controlled Phase: Placebo

Arm description:

Participants received 2 capsules of placebo (matched to laquinimod 0.6 mg) once daily orally for up to 24 months.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to laquinimod as per the schedule specified in the respective arms.

Arm title	Placebo-Controlled Phase: Laquinimod 0.6 mg

Arm description:

Participants received 1 capsule of laquinimod 0.6 mg and 1 capsule of matching placebo once daily orally for up to 24 months.

Arm type	Experimental
Investigational medicinal product name	Laquinimod
Investigational medicinal product code	TV-5600
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Laquinimod as per the dose and schedule specified in the respective arms.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to laquinimod as per the schedule specified in the respective arms.

Arm title	Placebo-Controlled Phase: Laquinimod 1.2 mg

Arm description:

Participants received laquinimod 1.2 mg (2 capsules of laquinimod 0.6 mg each) once daily orally for up

to 24 months.

Arm type	Experimental
Investigational medicinal product name	Laquinimod
Investigational medicinal product code	TV-5600
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Laquinimod as per the dose and schedule specified in the respective arms.

Number of subjects in period 1	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg
Started	740	727	732
Completed	596	623	532
Not completed	144	104	200
Adverse event, serious fatal	2	1	1
Consent withdrawn by subject	88	68	154
Adverse event, non-fatal	8	13	9
Pregnancy	12	5	9
Other than specified	11	9	10
Lost to follow-up	10	4	9
Noncompliance with drug administration	2	1	6
Lack of efficacy	10	3	2
Protocol deviation	1	-	-

Period 2

Period 2 title	Active Treatment Phase (24 Months)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Active Treatment Phase: Laquinimod 0.6 mg

Arm description:

Participants who completed the placebo-controlled phase on placebo and on laquinimod 0.6 mg treatment group after 01 January 2016, received 1 capsule of laquinimod 0.6 mg and 1 capsule of matching placebo once daily orally for 24 months.

Arm type	Experimental

Investigational medicinal product name	Laquinimod
Investigational medicinal product code	TV-5600
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Laquinimod as per the dose and schedule specified in the respective arms.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to laquinimod as per the schedule specified in the respective arms.

Arm title	Active Treatment Phase: Laquinimod 1.2 mg

Arm description:

Participants who completed the placebo-controlled phase on placebo and on laquinimod 1.2 mg treatment group prior to 01 January 2016, received laquinimod 1.2 mg (2 capsules of laquinimod 0.6 mg each) once daily orally for 24 months.

Arm type	Experimental
Investigational medicinal product name	Laquinimod
Investigational medicinal product code	TV-5600
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Laquinimod as per the dose and schedule specified in the respective arms.

Arm title	Active Treatment Phase: Off Drug

Arm description:

Participants who were discontinued from treatment with laquinimod 1.2 mg during the placebo-controlled phase due to sponsor decision after 01 January 2016 continued to the active-treatment phase off drug for 24 months.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2[1]	Active Treatment Phase: Laquinimod 0.6 mg	Active Treatment Phase: Laquinimod 1.2 mg	Active Treatment Phase: Off Drug
Started	891	504	215
Completed	7	10	0
Not completed	884	494	215
Adverse event, serious fatal	2	-	-
Consent withdrawn by subject	58	220	32
Adverse event, non-fatal	4	1	-
Pregnancy	2	5	2
Study terminated by sponsor	809	243	174
Other than specified	1	5	2

Lost to follow-up	5	11	1
Lack of efficacy	3	1	2
Noncompliance	-	4	2
Participant withdrew per Sponsor request	-	4	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: All participants who completed Period 1, did not continue to Period 2.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo-Controlled Phase: Placebo
Reporting group description:	
Participants received 2 capsules of placebo (matched to laquinimod 0.6 mg) once daily orally for up to 24 months.	
Reporting group title	Placebo-Controlled Phase: Laquinimod 0.6 mg
Reporting group description:	
Participants received 1 capsule of laquinimod 0.6 mg and 1 capsule of matching placebo once daily orally for up to 24 months.	
Reporting group title	Placebo-Controlled Phase: Laquinimod 1.2 mg
Reporting group description:	
Participants received laquinimod 1.2 mg (2 capsules of laquinimod 0.6 mg each) once daily orally for up to 24 months.	

Reporting group values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg
Number of subjects	740	727	732
Age categorical			
Units: Subjects			
Adults (18-64 years)	740	727	732
Age Continuous			
Units: years			
arithmetic mean	35.9	36.8	36.1
standard deviation	± 8.95	± 9.25	± 9.22
Sex: Female, Male			
Units: Subjects			
Female	488	510	475
Male	252	217	257
Race			
Units: Subjects			
White	724	712	717
Black	3	3	3
Asian	3	2	3
Other	10	8	9
Missing	0	2	0
Kurtzke's Expanded Disability Status Scale (EDSS) Score			
EDSS assesses disability in 8 functional systems with an overall score ranging from 0 (normal) to 10 (death due to multiple sclerosis [MS]).			
Units: Subjects			
Less than or equal to (<=) 4.0	653	635	644
Greater than (>) 4.0	87	90	88
Missing	0	2	0
Normalized Brain Volume			
This characteristic was analysed for a total of 2187 participants (Placebo [737], Laquinimod 0.6 mg [722], and Laquinimod 1.2 mg [728])			
Units: milliliters (mL)			
arithmetic mean	1437.2	1433.0	1434.4

standard deviation	± 93.37	± 92.49	± 93.41

Reporting group values	Total		
Number of subjects	2199		
Age categorical Units: Subjects			
Adults (18-64 years)	2199		
Age Continuous Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Subjects			
Female	1473		
Male	726		
Race Units: Subjects			
White	2153		
Black	9		
Asian	8		
Other	27		
Missing	2		
Kurtzke's Expanded Disability Status Scale (EDSS) Score			
EDSS assesses disability in 8 functional systems with an overall score ranging from 0 (normal) to 10 (death due to multiple sclerosis [MS]).			
Units: Subjects			
Less than or equal to (<=) 4.0	1932		
Greater than (>) 4.0	265		
Missing	2		
Normalized Brain Volume			
This characteristic was analysed for a total of 2187 participants (Placebo [737], Laquinimod 0.6 mg [722], and Laquinimod 1.2 mg [728])			
Units: milliliters (mL) arithmetic mean standard deviation	 -		

End points

End points reporting groups

Reporting group title	Placebo-Controlled Phase: Placebo
Reporting group description:	
Participants received 2 capsules of placebo (matched to laquinimod 0.6 mg) once daily orally for up to 24 months.	
Reporting group title	Placebo-Controlled Phase: Laquinimod 0.6 mg
Reporting group description:	
Participants received 1 capsule of laquinimod 0.6 mg and 1 capsule of matching placebo once daily orally for up to 24 months.	
Reporting group title	Placebo-Controlled Phase: Laquinimod 1.2 mg
Reporting group description:	
Participants received laquinimod 1.2 mg (2 capsules of laquinimod 0.6 mg each) once daily orally for up to 24 months.	
Reporting group title	Active Treatment Phase: Laquinimod 0.6 mg
Reporting group description:	
Participants who completed the placebo-controlled phase on placebo and on laquinimod 0.6 mg treatment group after 01 January 2016, received 1 capsule of laquinimod 0.6 mg and 1 capsule of matching placebo once daily orally for 24 months.	
Reporting group title	Active Treatment Phase: Laquinimod 1.2 mg
Reporting group description:	
Participants who completed the placebo-controlled phase on placebo and on laquinimod 1.2 mg treatment group prior to 01 January 2016, received laquinimod 1.2 mg (2 capsules of laquinimod 0.6 mg each) once daily orally for 24 months.	
Reporting group title	Active Treatment Phase: Off Drug
Reporting group description:	
Participants who were discontinued from treatment with laquinimod 1.2 mg during the placebo-controlled phase due to sponsor decision after 01 January 2016 continued to the active-treatment phase off drug for 24 months.	

Primary: Placebo-Controlled Phase: Time to Confirmed Disease Progression (CDP) Confirmed After At Least 3 Months (Number of Participants with CDP After At Least 3 Months)

End point title	Placebo-Controlled Phase: Time to Confirmed Disease Progression (CDP) Confirmed After At Least 3 Months (Number of Participants with CDP After At Least 3 Months)
End point description:	
Time to CDP was defined as the time to a sustained increase in Kurtzke's Expanded Disability Status Scale (EDSS) score of at least 1 point if baseline EDSS score was less than or equal to 5.0, or at least 0.5 point if the baseline EDSS score was 5.5, over a period of at least three months. EDSS assesses disability in 8 functional systems with an overall score ranging from 0 (normal) to 10 (death due to multiple sclerosis [MS]). Data is presented as distribution of CDP (number of participants with CDP) sustained for 3 months. Intent-to-treat (ITT) analysis set included all randomized participants.	
End point type	Primary
End point timeframe:	
Baseline to Month 24	

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	740	727	732	
Units: participants	73	66	69	

Statistical analyses

Statistical analysis title	Laquinimod 0.6 mg vs. Placebo

Statistical analysis description:

The primary analysis for the comparison between laquinimod 0.6 mg versus placebo was conducted using the baseline adjusted Cox proportional hazards model. Categorical EDSS at baseline (less than or equal to [<=] 4 or greater than [>] 4), country/geographical region (CGR), categorical age at baseline (<=38 or >38), and T2 volume at baseline were included as covariates in the model.

Comparison groups	Placebo-Controlled Phase: Placebo v Placebo-Controlled Phase: Laquinimod 0.6 mg
Number of subjects included in analysis	1467
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7057 [1]
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.937
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.668
upper limit	1.313

Notes:

[1] - Threshold for significance at 0.05 level.

Secondary: Placebo-Controlled Phase: Percent Change From Baseline in Brain Volume at Month 15

End point title	Placebo-Controlled Phase: Percent Change From Baseline in Brain Volume at Month 15

End point description:

Brain atrophy was defined by the percent change in brain volume from baseline to Month 15. The modified intent-to-treat 1 (mITT1) analysis set included data from all randomized participants at the Month 15 visit. For participants who prematurely discontinued treatment or completed the placebo-controlled phase before Month 15, the last available measurement was used, provided it was performed at least 9 months following the initiation of study drug. Here, 'Number of participants analyzed' = Participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline, Month 15

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	619	636	616	
Units: percent change				
arithmetic mean (standard deviation)	-0.8 (± 1.02)	-0.4 (± 1.01)	-0.4 (± 1.05)	

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-Controlled Phase: Time to First Confirmed Relapse (Number of Participants with Confirmed Relapse)

End point title	Placebo-Controlled Phase: Time to First Confirmed Relapse (Number of Participants with Confirmed Relapse)

End point description:

Relapse was defined as appearance of one or more new neurological abnormalities or reappearance or worsening of one or more previously observed neurological abnormalities, lasting for at least 48 hours (in absence of fever or any infection) and immediately preceded by an improving neurological state of at least 30 days from onset of previous relapse. An event was counted as a relapse only when the participant's symptoms were accompanied by observed objective neurological changes, consistent with an increase of at least 0.5 in EDSS; or one grade in score of 2 or more of 7 Functional Systems (FS) (excluding changes in bowel or bladder function or cognition); or 2 grades in score of one of the FS as compared to previous evaluation. EDSS assesses disability in 8 FS with an overall score ranging from 0 (normal) to 10 (death due to MS). Data is presented as distribution of relapsing participants (number of participants with confirmed relapse). ITT analysis set: all randomized participants.

End point type	Secondary

End point timeframe:

Baseline to Month 24

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	740	727	732	
Units: participants	332	269	222	

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-Controlled Phase: Time to CDP Confirmed After At Least 6 Months (Number of Participants with CDP After At Least 6 Months)

End point title	Placebo-Controlled Phase: Time to CDP Confirmed After At

	Least 6 Months (Number of Participants with CDP After At Least 6 Months)

End point description:

Time to CDP was defined as the time to a sustained increase in Kurtzke's EDSS score of at least 1 point if baseline EDSS score was less than or equal to 5.0, or at least 0.5 point if the baseline EDSS score was 5.5, over a period of at least 6 months. EDSS assesses disability in 8 functional systems with an overall score ranging from 0 (normal) to 10 (death due to MS). Data is presented as distribution of CDP (number of participants with CDP) sustained for 6 months. ITT analysis set included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline to Month 24

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	740	727	732	
Units: participants				
number (not applicable)	49	49	51	

Statistical analyses

No statistical analyses for this end point

Secondary: Placebo-Controlled Phase: Time to CDP Confirmed After At Least 9 Months (Number of Participants with Confirmed Relapse After At Least 9 Months)

End point title	Placebo-Controlled Phase: Time to CDP Confirmed After At Least 9 Months (Number of Participants with Confirmed Relapse After At Least 9 Months)

End point description:

Time to CDP was defined as the time to a sustained increase in Kurtzke's EDSS score of at least 1 point if baseline EDSS score was less than or equal to 5.0, or at least 0.5 point if the baseline EDSS score was 5.5, over a period of at least 9 months. EDSS assesses disability in 8 functional systems with an overall score ranging from 0 (normal) to 10 (death due to MS). Data is presented as distribution of CDP (number of participants with CDP) sustained for 9 months. ITT analysis set included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline to Month 24

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	740	727	732	
Units: participants	38	38	39	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Placebo-Controlled Phase: Number of Participants With Adverse Events (AEs)

End point title	Placebo-Controlled Phase: Number of Participants With Adverse Events (AEs)

End point description:

An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. Serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. AEs included both SAEs and non-serious AEs. Safety analysis set included all participants who were randomized and received at least one dose of study drug.

End point type	Other pre-specified

End point timeframe:

Baseline up to Month 24

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	740	727	732	
Units: participants	546	565	575	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Active-Treatment Phase: Number of Participants With AEs

End point title	Active-Treatment Phase: Number of Participants With AEs

End point description:

An AE was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. AEs included both SAEs and non-serious AEs. Safety analysis set in active-treatment phase included all

participants who completed placebo-controlled phase on treatment and continued to either of the 2 laquinimod treatments during active-treatment phase.

End point type	Other pre-specified

End point timeframe:

Baseline (Month 0 of active-treatment phase/Month 24 of placebo-controlled phase) up to Month 24 of active-treatment phase

End point values	Active Treatment Phase: Laquinimod 0.6 mg	Active Treatment Phase: Laquinimod 1.2 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	891	504		
Units: participants	442	241		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Placebo-Controlled Phase: Number of Participants With Clinically Significant Vital Signs Abnormalities

End point title	Placebo-Controlled Phase: Number of Participants With Clinically Significant Vital Signs Abnormalities

End point description:

Clinically significant vital signs abnormalities included: Pulse rate: greater than or equal to (>=) 120 beats per minute (bpm) and increase from baseline of >=30 bpm, <=45 bpm and decrease from baseline of >=30 bpm; Systolic blood pressure: >=180 millimeters of mercury (mmHg) and increase from baseline of >=30 mmHg, <=90 and decrease from baseline of >=30 mmHg; Diastolic blood pressure: >=100 mmHg and increase from baseline of >=20 mmHg, <=50 mmHg and decrease from baseline of >=20 mmHg. Safety analysis set included all participants who were randomized and received at least one dose of study drug.

End point type	Other pre-specified

End point timeframe:

Baseline up to Week 24

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	740	727	732	
Units: participants	21	21	29	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Active-Treatment Phase: Number of Participants With Clinically Significant Vital Signs Abnormalities

End point title	Active-Treatment Phase: Number of Participants With Clinically Significant Vital Signs Abnormalities

End point description:

Clinically significant vital signs abnormalities included: Pulse rate: >=120 bpm and increase from baseline of >=30 bpm, <=45 bpm and decrease from baseline of >=30 bpm; Systolic blood pressure: >=180 mmHg and increase from baseline of >=30 mmHg, <=90 and decrease from baseline of >=30 mmHg; Diastolic blood pressure: >=100 mmHg and increase from baseline of >=20 mmHg, <=50 mmHg and decrease from baseline of >=20 mmHg. Safety analysis set in active-treatment phase included all participants who completed placebo-controlled phase on treatment and continued to either of the 2 laquinimod treatments during active-treatment phase.

End point type	Other pre-specified

End point timeframe:

Baseline (Month 0 of active-treatment phase/Month 24 of placebo-controlled phase) up to Month 24 of active-treatment phase

End point values	Active Treatment Phase: Laquinimod 0.6 mg	Active Treatment Phase: Laquinimod 1.2 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	891	504		
Units: participants	17	7		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Placebo-Controlled Phase: Number of Participants With Shift From Baseline to Endpoint in Electrocardiogram (ECG) Parameters

End point title	Placebo-Controlled Phase: Number of Participants With Shift From Baseline to Endpoint in Electrocardiogram (ECG) Parameters

End point description:

ECG parameters included: PR interval, QRS interval, QT interval corrected using the Fridericia formula (QTcF) and QT interval corrected using the Bazett's formula (QTcB). Shifts represented as Baseline - endpoint value (last observed post-baseline value). Abnormal NCS indicated an abnormal but not clinically significant finding. Abnormal CS indicated an abnormal and clinically significant finding. Safety analysis set included all participants who were randomized and received at least one dose of study drug. Here, 'Number of participants analysed=participants evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline, Endpoint (Month 24)

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	734	723	724	
Units: participants				
Normal - Normal	463	467	470	
Normal - Abnormal NCS	139	124	126	
Normal - Abnormal CS	0	6	5	
Abnormal NCS - Normal	32	27	28	
Abnormal NCS - Abnormal NCS	98	96	90	
Abnormal NCS - Abnormal CS	1	1	2	
Abnormal CS - Normal	0	1	0	
Abnormal CS - Abnormal NCS	0	0	0	
Abnormal CS - Abnormal CS	1	1	3	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Active Treatment Phase: Number of Participants With Shift From Baseline to Endpoint in ECG Parameters

End point title	Active Treatment Phase: Number of Participants With Shift From Baseline to Endpoint in ECG Parameters

End point description:

ECG parameters included: PR interval, QRS interval, QTcF and QTcB. Shifts represented as Baseline - endpoint value (last observed post-baseline value). Abnormal NCS indicated an abnormal but not clinically significant finding. Abnormal CS indicated an abnormal and clinically significant finding. Safety analysis set in active-treatment phase included all participants who completed placebo-controlled phase on treatment and continued to either of the 2 laquinimod treatments during active-treatment phase and had ECG shift from baseline data available.

End point type	Other pre-specified

End point timeframe:

Baseline (Month 0 of active-treatment phase/Month 24 of placebo-controlled phase), endpoint (Month 24 of active-treatment phase)

End point values	Active Treatment Phase: Laquinimod 0.6 mg	Active Treatment Phase: Laquinimod 1.2 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	888	501		
Units: participants				
Normal – Normal	641	353		

Normal - Abnormal NCS	137	80		
Normal - Abnormal CS	7	5		
Abnormal NCS – Normal	18	17		
Abnormal NCS - Abnormal NCS	81	45		
Abnormal NCS - Abnormal CS	4	0		
Abnormal CS – Normal	0	0		
Abnormal CS - Abnormal NCS	0	0		
Abnormal CS - Abnormal CS	0	1		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Placebo-Controlled Phase: Number of Participants With Potentially Clinically Significant Abnormal Serum Chemistry

End point title	Placebo-Controlled Phase: Number of Participants With Potentially Clinically Significant Abnormal Serum Chemistry

End point description:

Potentially clinically significant serum chemistry abnormalities included: Glucose <=3 and >=13.88 millimoles per liter (mmol/L); Alanine aminotransferase (ALT) (in units per liter [U/L]), aspartate aminotransferase (AST) (in U/L), alkaline phosphatase (in U/L), gamma-glutamyltransferase (GGT) (in U/L), creatine phosphokinase (CPK) (in U/L), C-reactive protein (CRP) (in milligrams per liter [mg/L]), pancreatic amylase (in U/L)>=3 * upper limit of normal (ULN); Fibrinogen >=6 grams per liter (gm/L); Sodium <=130 and >=150 mmol/L; Potassium <=3.2 and >=5.5 mmol/L; Calcium <=1.87 and >=2.75 mmol/L; Phosphate <=0.65 and >=1.61 mmol/L. Safety analysis set included all participants who were randomized and received at least one dose of study drug. Here, 'Number of participants analysed'=participants evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline up to Month 24

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	736	723	724	
Units: participants	157	165	187	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Active Treatment Phase: Number of Participants With Potentially Clinically Significant Abnormal Serum Chemistry

End point title	Active Treatment Phase: Number of Participants With Potentially Clinically Significant Abnormal Serum Chemistry

End point description:

Potentially clinically significant serum chemistry abnormalities included: Glucose <=3 and >=13.88 mmol/L; ALT (in U/L), AST (in U/L), alkaline phosphatase (in U/L), GGT (in U/L), CPK (in U/L), CRP (in mg/L), pancreatic amylase (in U/L)>=3 * ULN; Fibrinogen >=6 gm/L; Sodium <=130 and >=150 mmol/L; Potassium <=3.2 and >=5.5 mmol/L; Calcium <=1.87 and >=2.75 mmol/L; Phosphate <=0.65 and >=1.61 mmol/L; Blood urea nitrogen (in mmol/L); Total bilirubin >=28 micromols per liter (micromols/L); Creatinine >=117 micromols/L; Albumin <=25 gm/L. Safety analysis set in active-treatment phase included all participants who completed placebo-controlled phase on treatment and continued to either of the 2 laquinimod treatments during active-treatment phase.

End point type	Other pre-specified

End point timeframe:

Baseline (Month 0 of active-treatment phase/Month 24 of placebo-controlled phase) up to Month 24 of active-treatment phase

End point values	Active Treatment Phase: Laquinimod 0.6 mg	Active Treatment Phase: Laquinimod 1.2 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	891	504		
Units: participants	887	501		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Placebo-Controlled Phase: Number of Participants With Potentially Clinically Significant Abnormal Hematology Values

End point title	Placebo-Controlled Phase: Number of Participants With Potentially Clinically Significant Abnormal Hematology Values

End point description:

Potentially clinically significant hematological abnormalities included: Hemoglobin <=11.5 grams per deciliter (gm/dL) in males and <=10 gm/dL in females; White blood cells (WBCs) count <=2.5 and >=21*10^9 per liter (L); Absolute neutrophil count (ANC) <=1.49*10^9 per L; Platelet count <=100 and >=600*10^9 per L. Safety analysis set included all participants who were randomized and received at least one dose of study drug. Here, 'Number of participants analysed'=participants evaluable for this endpoint.

End point type	Other pre-specified

End point timeframe:

Baseline up to Month 24

End point values	Placebo-Controlled Phase: Placebo	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	735	723	723	
Units: participants	71	78	83	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Active Treatment Phase: Number of Participants With Potentially Clinically Significant Abnormal Hematology Values

End point title	Active Treatment Phase: Number of Participants With Potentially Clinically Significant Abnormal Hematology Values

End point description:

Potentially clinically significant hematological abnormalities included: Hemoglobin <=11.5, >=20 gm/dL in males, and <=10, >=18.5 gm/dL in females; WBCs count <=2.5 and >=21*10^9 per L; ANC <=1.49*10^9 per L; Platelet count <=100 and >=600*10^9 per L. Safety analysis set in active-treatment phase included all participants who completed placebo-controlled phase on treatment and continued to either of the 2 laquinimod treatments during active-treatment phase.

End point type	Other pre-specified

End point timeframe:

Baseline (Month 0 of active-treatment phase/Month 24 of placebo-controlled phase) up to Month 24 of active-treatment phase

End point values	Active Treatment Phase: Laquinimod 0.6 mg	Active Treatment Phase: Laquinimod 1.2 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	891	504		
Units: participants	886	499		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected for the procedure and at each follow-up visit at 2 weeks, 6 weeks, 12 weeks, 24 weeks, and 52 weeks post-treatment

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Placebo-Controlled Phase: Laquinimod 0.6 mg

Reporting group description:

Participants received 1 capsule of laquinimod 0.6 mg and 1 capsule of matching placebo once daily orally for up to 24 months.

Reporting group title	Placebo-Controlled Phase: Laquinimod 1.2 mg

Reporting group description:

Participants received laquinimod 1.2 mg (2 capsules of laquinimod 0.6 mg each) once daily orally for up to 24 months.

Reporting group title	Active Treatment Phase: Early Laquinimod 0.6 mg

Reporting group description:

Participants who completed the placebo-controlled phase on laquinimod 0.6 mg treatment group after 01 January 2016, received 1 capsule of laquinimod 0.6 mg and 1 capsule of matching placebo once daily orally for 24 months.

Reporting group title	Placebo-Controlled Phase: Placebo

Reporting group description:

Participants received 2 capsules of placebo (matched to laquinimod 0.6 mg) once daily orally for up to 24 months.

Reporting group title	Active Treatment Phase: Early Laquinimod 1.2 mg

Reporting group description:

Participants who completed the placebo-controlled phase on laquinimod 1.2 mg treatment group prior to 01 January 2016, received laquinimod 1.2 mg (2 capsules of laquinimod 0.6 mg each) once daily orally for 24 months.

Reporting group title	Active Treatment Phase: Off Drug

Reporting group description:

Participants who were discontinued from treatment with laquinimod 1.2 mg during the placebo-controlled phase due to sponsor decision after 01 January 2016, continued to the active-treatment phase off drug for 24 months.

Reporting group title	Active Treatment Phase: From Placebo to Laquinimod 1.2 mg

Reporting group description:

Participants who completed the placebo-controlled phase on placebo treatment group prior to 01 January 2016, received laquinimod 1.2 mg (2 capsules of laquinimod 0.6 mg each) once daily orally for 24 months.

Reporting group title	Active Treatment Phase: From Placebo to Laquinimod 0.6 mg

Reporting group description:

Participants who completed the placebo-controlled phase on placebo treatment group after 01 January 2016, received 1 capsule of laquinimod 0.6 mg and 1 capsule of matching placebo once daily orally for 24 months.

Serious adverse events	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	Active Treatment Phase: Early Laquinimod 0.6 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 727 (7.84%)	49 / 732 (6.69%)	24 / 580 (4.14%)
number of deaths (all causes)	1	1	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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 breast neoplasm			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign neoplasm of adrenal gland			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Fibroadenoma of breast			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Haemangioma			

subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 chest wall			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papilloma			
subjects affected / exposed	1 / 727 (0.14%)	1 / 732 (0.14%)	0 / 580 (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
Salivary gland adenoma			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Thyroid cancer			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Uterine leiomyoma			
subjects affected / exposed	5 / 727 (0.69%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone sarcoma			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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			
Deep vein thrombosis			

subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Embolism arterial			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Vasculitis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Venous thrombosis limb			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Surgical and medical procedures			
Hospitalisation			

subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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	1 / 727 (0.14%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal growth abnormality			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Unintended pregnancy			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion			
subjects affected / exposed	0 / 727 (0.00%)	2 / 732 (0.27%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion missed			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Abortion threatened			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fatigue			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Pyrexia			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Strangulated hernia			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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			
Drug hypersensitivity			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoidosis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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			
Acquired hydrocele			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Adnexal torsion			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix disorder			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Fallopian tube cyst			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Menometrorrhagia			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Metrorrhagia			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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	1 / 727 (0.14%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian haemorrhage			
subjects affected / exposed	1 / 727 (0.14%)	1 / 732 (0.14%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polycystic ovaries			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 disorder			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Nasal septum deviation			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Pneumothorax spontaneous			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Vasomotor rhinitis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Bronchiectasis			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Psychiatric disorders			

Acute psychosis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Affective disorder			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Confusional state			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Major depression			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Persecutory delusion			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Personality change due to a general medical condition			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Suicidal ideation			

subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Suicide attempt			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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			
Alpha 1 foetoprotein abnormal			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Nuclear magnetic resonance imaging brain abnormal			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Injury, poisoning and procedural			

complications			
Ankle fracture			
subjects affected / exposed	0 / 727 (0.00%)	2 / 732 (0.27%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone contusion			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Brain contusion			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cartilage injury			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Femur fracture			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			

subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Meniscus injury			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Poisoning deliberate			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Postoperative adhesion			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Pubis fracture			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	2 / 727 (0.28%)	1 / 732 (0.14%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fractured base			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Toxicity to various agents			
subjects affected / exposed	1 / 727 (0.14%)	1 / 732 (0.14%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Traumatic liver injury			

subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Ulna fracture			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Intentional overdose			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 727 (0.00%)	4 / 732 (0.55%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	1 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Angina pectoris			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Atrial fibrillation			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			

subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cardiovascular insufficiency			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Coronary artery occlusion			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Myocardial infarction			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	2 / 580 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Myocardial ischaemia			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Coma			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 neuropathy			

subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Ischaemic stroke			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Multiple sclerosis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis relapse			
subjects affected / exposed	2 / 727 (0.28%)	1 / 732 (0.14%)	2 / 580 (0.34%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological decompensation			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Neuromyelitis optica spectrum disorder			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Psychomotor hyperactivity			

subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	1 / 727 (0.14%)	1 / 732 (0.14%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Hypochromic anaemia			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Lymphadenitis			

subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 727 (0.14%)	1 / 732 (0.14%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 pain			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Coeliac disease			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal perforation			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Gastric polyps			

subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Gastritis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Gastrointestinal inflammation			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Inguinal hernia			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic necrosis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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	0 / 727 (0.00%)	4 / 732 (0.55%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Pancreatitis chronic			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Periodontal inflammation			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Peritoneal adhesions			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Peritoneal haemorrhage			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Autoimmune pancreatitis			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Ileus			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 727 (0.00%)	3 / 732 (0.41%)	0 / 580 (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
Cholecystitis acute			

subjects affected / exposed	2 / 727 (0.28%)	0 / 732 (0.00%)	0 / 580 (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
Cholecystitis chronic			
subjects affected / exposed	2 / 727 (0.28%)	0 / 732 (0.00%)	0 / 580 (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
Cholelithiasis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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 obstructive			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Cholestasis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis cholestatic			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Hepatotoxicity			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Hepatitis toxic			

subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 727 (0.28%)	0 / 732 (0.00%)	0 / 580 (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
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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			
Ankylosing spondylitis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Cervical spinal stenosis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Femoroacetabular impingement			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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 chest pain			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Neck pain			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Osteoarthritis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Osteonecrosis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	1 / 727 (0.14%)	1 / 732 (0.14%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess oral			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			

subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
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 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Cholecystitis infective			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic tonsillitis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Endometritis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Enterovirus infection			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Erysipelas			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Helicobacter gastritis			

subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Hepatitis B			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Herpes zoster oticus			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Infected dermal cyst			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 abscess			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Pneumonia			
subjects affected / exposed	2 / 727 (0.28%)	2 / 732 (0.27%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			

subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Pyelonephritis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Pyelonephritis chronic			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Salpingitis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salpingo-oophoritis			
subjects affected / exposed	2 / 727 (0.28%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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 bladder abscess			

subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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 tract infection			
subjects affected / exposed	1 / 727 (0.14%)	1 / 732 (0.14%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine infection			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis viral			
subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Tuberculosis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	0 / 580 (0.00%)
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 inadequate control			
subjects affected / exposed	0 / 727 (0.00%)	0 / 732 (0.00%)	1 / 580 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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
Metabolic disorder			

subjects affected / exposed	0 / 727 (0.00%)	1 / 732 (0.14%)	0 / 580 (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
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 727 (0.14%)	0 / 732 (0.00%)	0 / 580 (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	Placebo-Controlled Phase: Placebo	Active Treatment Phase: Early Laquinimod 1.2 mg	Active Treatment Phase: Off Drug
Total subjects affected by serious adverse events			
subjects affected / exposed	43 / 740 (5.81%)	10 / 268 (3.73%)	5 / 215 (2.33%)
number of deaths (all causes)	2	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 breast neoplasm			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 neoplasm of adrenal gland			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 lymphocytic leukaemia			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Clear cell renal cell carcinoma			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 / 740 (0.00%)	0 / 268 (0.00%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to chest wall			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papilloma			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland adenoma			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Uterine leiomyoma			

subjects affected / exposed	2 / 740 (0.27%)	0 / 268 (0.00%)	0 / 215 (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
Bone sarcoma			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism arterial			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Vasculitis			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	2 / 740 (0.27%)	0 / 268 (0.00%)	0 / 215 (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
Foetal growth abnormality			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Unintended pregnancy			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion missed			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abortion threatened			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
Asthenia			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Fatigue			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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-cardiac chest pain			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Strangulated hernia			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sarcoidosis			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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			
Acquired hydrocele			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Adnexal torsion			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix disorder			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fallopian tube cyst			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Menometrorrhagia			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metrorrhagia			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polycystic ovaries			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Interstitial lung disease			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Lung disorder			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Pleurisy			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vasomotor rhinitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
Acute psychosis			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Affective disorder			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Persecutory delusion			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Personality change due to a general medical condition			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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

Psychotic disorder			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Schizophrenia			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Completed suicide			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
Alpha 1 foetoprotein abnormal			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nuclear magnetic resonance imaging brain abnormal			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone contusion			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain contusion			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Cartilage injury			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Fall			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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

Femoral neck fracture			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Jaw fracture			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Poisoning deliberate			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative adhesion			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Road traffic accident			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Skull fractured base			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Subdural haematoma			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Thermal burn			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Thoracic vertebral fracture			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic liver injury			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Intentional overdose			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 myocardial infarction			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiovascular insufficiency			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery occlusion			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 infarction			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
Altered state of consciousness			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Diabetic neuropathy			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 stroke			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Multiple sclerosis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis relapse			
subjects affected / exposed	7 / 740 (0.95%)	1 / 268 (0.37%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	1 / 7	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological decompensation			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuromyelitis optica spectrum disorder			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor hyperactivity			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 epilepticus			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Blood and lymphatic system disorders			
Hypochromic anaemia			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 thrombocytopenic purpura			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	2 / 740 (0.27%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Thrombocytopenia			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coeliac disease			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal perforation			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 polyps			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Gastritis erosive			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 inflammation			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic necrosis			

subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Pancreatitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 acute			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 chronic			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periodontal inflammation			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal adhesions			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritoneal haemorrhage			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune pancreatitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	2 / 740 (0.27%)	0 / 268 (0.00%)	0 / 215 (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
Cholelithiasis obstructive			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Hepatitis cholestatic			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
Urticaria			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
Nephrolithiasis			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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			
Ankylosing spondylitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical spinal stenosis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Femoroacetabular impingement			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Musculoskeletal chest pain			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 oral			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Chronic tonsillitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometritis			
subjects affected / exposed	2 / 740 (0.27%)	0 / 268 (0.00%)	0 / 215 (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
Enterovirus infection			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Helicobacter gastritis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis B			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 zoster oticus			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected dermal cyst			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 abscess			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 740 (0.14%)	1 / 268 (0.37%)	0 / 215 (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
Pilonidal cyst			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 chronic			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salpingitis			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Salpingo-oophoritis			
subjects affected / exposed	2 / 740 (0.27%)	0 / 268 (0.00%)	0 / 215 (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
Sepsis			

subjects affected / exposed	0 / 740 (0.00%)	1 / 268 (0.37%)	0 / 215 (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
Sinusitis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 bladder abscess			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 tract infection			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 infection			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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
Hepatitis viral			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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			
Diabetes mellitus			
subjects affected / exposed	1 / 740 (0.14%)	0 / 268 (0.00%)	0 / 215 (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 inadequate control			

subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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 ketoacidosis			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic disorder			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 740 (0.00%)	0 / 268 (0.00%)	0 / 215 (0.00%)
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	Active Treatment Phase: From Placebo to Laquinimod 1.2 mg	Active Treatment Phase: From Placebo to Laquinimod 0.6 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 236 (3.81%)	5 / 311 (1.61%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign breast neoplasm			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of adrenal gland			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemangioma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to chest wall			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papilloma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary gland adenoma			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone sarcoma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism arterial			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hospitalisation			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal growth abnormality			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unintended pregnancy			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abortion			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion missed			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion threatened			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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			
Asthenia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Strangulated hernia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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			
Drug hypersensitivity			
subjects affected / exposed	0 / 236 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sarcoidosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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			
Acquired hydrocele			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adnexal torsion			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervix disorder			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fallopian tube cyst			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menometrorrhagia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metrorrhagia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian haemorrhage			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycystic ovaries			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pleurisy			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasomotor rhinitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Affective disorder			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Persecutory delusion			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Personality change due to a general medical condition			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alpha 1 foetoprotein abnormal			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nuclear magnetic resonance imaging brain abnormal			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone contusion			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cartilage injury			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 236 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning deliberate			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative adhesion			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis fracture			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fractured base			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic liver injury			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 myocardial infarction			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (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			
Altered state of consciousness			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis relapse			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological decompensation			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuromyelitis optica spectrum disorder			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychomotor hyperactivity			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Hypochromic anaemia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (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 pain			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Coeliac disease			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic necrosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontal inflammation			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal adhesions			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune pancreatitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis obstructive			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis cholestatic			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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			
Urticaria			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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			
Nephrolithiasis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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			
Ankylosing spondylitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoroacetabular impingement			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 oral			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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	1 / 236 (0.42%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic tonsillitis			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovirus infection			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster oticus			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	0 / 236 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian abscess			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingitis			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salpingo-oophoritis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder abscess			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine infection			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis viral			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			

subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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			
Diabetes mellitus			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic disorder			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 236 (0.00%)	0 / 311 (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	Placebo-Controlled Phase: Laquinimod 0.6 mg	Placebo-Controlled Phase: Laquinimod 1.2 mg	Active Treatment Phase: Early Laquinimod 0.6 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	262 / 727 (36.04%)	286 / 732 (39.07%)	102 / 580 (17.59%)
Investigations			
Amylase increased			

subjects affected / exposed	17 / 727 (2.34%)	38 / 732 (5.19%)	6 / 580 (1.03%)
occurrences (all)	20	43	7
Nervous system disorders			
Headache			
subjects affected / exposed	122 / 727 (16.78%)	131 / 732 (17.90%)	22 / 580 (3.79%)
occurrences (all)	238	227	38
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 727 (3.85%)	43 / 732 (5.87%)	22 / 580 (3.79%)
occurrences (all)	32	50	25
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	54 / 727 (7.43%)	85 / 732 (11.61%)	12 / 580 (2.07%)
occurrences (all)	74	110	14
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	63 / 727 (8.67%)	60 / 732 (8.20%)	40 / 580 (6.90%)
occurrences (all)	90	86	52
Respiratory tract infection viral			
subjects affected / exposed	32 / 727 (4.40%)	31 / 732 (4.23%)	14 / 580 (2.41%)
occurrences (all)	54	37	19

Non-serious adverse events	Placebo-Controlled Phase: Placebo	Active Treatment Phase: Early Laquinimod 1.2 mg	Active Treatment Phase: Off Drug
Total subjects affected by non-serious adverse events			
subjects affected / exposed	243 / 740 (32.84%)	46 / 268 (17.16%)	35 / 215 (16.28%)
Investigations			
Amylase increased			
subjects affected / exposed	18 / 740 (2.43%)	2 / 268 (0.75%)	2 / 215 (0.93%)
occurrences (all)	19	2	2
Nervous system disorders			
Headache			
subjects affected / exposed	116 / 740 (15.68%)	8 / 268 (2.99%)	10 / 215 (4.65%)
occurrences (all)	222	14	13
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	30 / 740 (4.05%)	13 / 268 (4.85%)	7 / 215 (3.26%)
occurrences (all)	35	16	7

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	39 / 740 (5.27%)	8 / 268 (2.99%)	9 / 215 (4.19%)
occurrences (all)	47	10	10
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	63 / 740 (8.51%)	14 / 268 (5.22%)	8 / 215 (3.72%)
occurrences (all)	91	20	13
Respiratory tract infection viral			
subjects affected / exposed	39 / 740 (5.27%)	7 / 268 (2.61%)	3 / 215 (1.40%)
occurrences (all)	56	9	3

Non-serious adverse events	Active Treatment Phase: From Placebo to Laquinimod 1.2 mg	Active Treatment Phase: From Placebo to Laquinimod 0.6 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 236 (18.22%)	43 / 311 (13.83%)	
Investigations			
Amylase increased			
subjects affected / exposed	5 / 236 (2.12%)	6 / 311 (1.93%)	
occurrences (all)	8	6	
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 236 (4.24%)	14 / 311 (4.50%)	
occurrences (all)	15	25	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 236 (3.81%)	9 / 311 (2.89%)	
occurrences (all)	12	9	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	12 / 236 (5.08%)	1 / 311 (0.32%)	
occurrences (all)	14	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	11 / 236 (4.66%)	11 / 311 (3.54%)	
occurrences (all)	13	13	
Respiratory tract infection viral			

subjects affected / exposed occurrences (all)	5 / 236 (2.12%) 6	3 / 311 (0.96%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 July 2013	Amendment 1 to the protocol was issued after 200 participants were enrolled in the study. Changes to the protocol were considered to have no negative impact on the safety of participants already enrolled into the study. The following major procedural changes (not all-inclusive) were made to the protocol: - Disease duration of at least 6 months but not more than 12 years was updated to disease duration of not more than 15 years. - Clarification regarding disallowed medications following early treatment discontinuation (ETD). - Fibrinogen was added to the battery of safety laboratory tests at all visits.
08 June 2014	Amendment 2 to the protocol was issued after 1566 participants were enrolled into the study. Changes to the protocol were considered to have no negative impact on the safety of participants already enrolled into the study. The following major procedural changes (not all-inclusive) were made to the protocol: An increase in sample size and change in the timing of blinded sample size reassessment due to faster than expected enrollment. - Implementation of more stringent pregnancy prevention measures. - Updates to the introduction and safety sections based on accumulating data with laquinimod.
24 February 2015	Amendment 3 to the protocol was issued after 2068 participants were enrolled into the study. Changes to the protocol were considered to have no negative impact on the safety of participants already enrolled into the study. The following major procedural changes (not all-inclusive) were made to the protocol: Change in study design to an event-driven analysis based on Food and Drug Administration (FDA) feedback. - Sample size clarification. - Change in timing of blinded sample size reassessment. - Requirement to perform abdominal computed tomography (CT) as soon as possible when pancreatitis is suspected based on DMC recommendation.
26 January 2016	Amendment 4 to protocol was issued after 2199 participants were enrolled into study. Changes to protocol were considered to have no negative impact on safety of participants already enrolled into study. As a result of data monitoring committee recommendation to stop all laquinimod treatment groups above 0.6 mg, the following major changes (not all-inclusive) were made to protocol: - Laquinimod 1.2-mg treatment group was discontinued. - All ongoing participants were asked to re-consent to a revised form that included information on cardiovascular risk findings at higher doses of laquinimod (1.2 and 1.5 mg). - All participants assigned to placebo treatment in placebo-controlled phase would start treatment with laquinimod 0.6 mg in active treatment phase. - Stopping rules were added for renal and hepatic impairment. - GFR monitoring (and measurement of weight) was to be performed at all visits to assess renal function. - Extra emphasis was placed on moderate/strong inhibitors of cytochrome P450 3A4 (CYP3A4) being disallowed. - Addition of cardiovascular risk assessment and management procedure. - Ischemic cardiac events and cerebrovascular events were now classed as protocol-defined adverse events for expedited reporting and were to be reported to sponsor within 48 hours, including completion of corresponding dedicated case report form. - Modification was made to statistical analyses to reflect discontinued laquinimod 1.2-mg treatment group. Laquinimod 1.2-mg treatment group was excluded from all inferential analyses and is presented only using descriptive statistics. - For hierarchical analysis of the primary endpoint and secondary endpoints using a gatekeeping approach, Hochberg-closed procedure was replaced with hierarchical approach for the 2 then-existing secondary endpoints, brain atrophy as defined by percent change in brain volume from baseline to month 15 and time to first confirmed relapse during placebo-controlled phase.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported