Clinical trial results:
A Multicenter, Open-Label, Extension Study to Evaluate the Long-Term Safety and Efficacy of BIIB019, Daclizumab High Yield Process (DAC HYP), Monotherapy in Subjects With Multiple Sclerosis Who Have Completed Study 205MS301

Summary

EudraCT number	2012-003176-39
Trial protocol	DE IT CZ HU PL SE ES IE GB FI GR FR DK
Global end of trial date	24 September 2018

Results information

Result version number	v2 (current)
This version publication date	27 November 2019
First version publication date	10 October 2019
Version creation reason	• Correction of full data set The EudraCT record is being updated to align with the updates made on ClinicalTrials.gov as a result of PRS Review comments.

Trial information

Trial identification

Sponsor protocol code	205MS303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01797965
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, Massachusetts, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 September 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the safety and tolerability of long-term treatment with BIIB019 (Daclizumab High Yield Process; DAC HYP) monotherapy in subjects with relapsing remitting multiple sclerosis (RRMS) who completed Study 205MS301 (NCT01064401), Study 205MS203 (NCT01051349) or Study 205MS302 (NCT01462318). Secondary objectives of this study in this study population are as follows: To describe MS-related outcomes, including MS relapse, disability progression, MS lesion formation, and subject-reported impact of MS, following long-term treatment with DAC HYP To assess the long-term immunogenicity of DAC HYP administered by prefilled syringe (PFS) To assess the safety, tolerability, and efficacy of switching to DAC HYP in subjects previously on long-term treatment with interferon β-1a (Avonex) in Study 205MS301(NCT01064401).

Protection of trial subjects:

Written informed consent was obtained from each subject prior to evaluations being performed for eligibility. Subjects were given adequate time to review the information in the informed consent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study. Through the informed consent process each subject was made aware of the purpose of the study, the procedures, the benefits and risks of the study, the discomforts and the precautions taken. Any side effects or other health issues occurring during the study were followed up by the study doctor. Subjects were able to stop taking part in the study at any time without giving any reason.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 February 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 413
Country: Number of subjects enrolled	Russian Federation: 175
Country: Number of subjects enrolled	United States: 114
Country: Number of subjects enrolled	Ukraine: 133
Country: Number of subjects enrolled	Serbia: 86
Country: Number of subjects enrolled	Czech Republic: 132
Country: Number of subjects enrolled	Italy: 57
Country: Number of subjects enrolled	United Kingdom: 61
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Germany: 30

Country: Number of subjects enrolled	Hungary: 67
Country: Number of subjects enrolled	Romania: 26
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Brazil: 19
Country: Number of subjects enrolled	India: 21
Country: Number of subjects enrolled	Argentina: 16
Country: Number of subjects enrolled	Greece: 13
Country: Number of subjects enrolled	Sweden: 16
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	Moldova, Republic of: 12
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Ireland: 7
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Georgia: 3
Country: Number of subjects enrolled	Switzerland: 3
Worldwide total number of subjects	1501
EEA total number of subjects	889

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)	1501
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled in the study at 226 investigative sites in 28 countries (United States, Canada, Western European countries, Australia, Israel, Eastern European countries, Argentina, Brazil, India, and Mexico) from 15 February 2013 to 24 September 2018.

Pre-assignment

Screening details:

Subjects who completed studies: 205MS301 (NCT01064401), 205MS203 (NCT01051349), 205MS302 (NCT01462318) were eligible to enroll in this long-term extension study.

Pre-assignment period milestones

Number of subjects started	1501
Number of subjects completed	1500

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Adverse event, non-fatal: 1

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)

Arm description:

Daclizumab High Yield Process (DAC HYP) 150 mg SC injection every 4 weeks for up to 4.6 years in this long-term extension study 303; includes subjects who previously received interferon beta-1a (IFN β-1a) 30 µg intramuscular (IM) injection once weekly in study 301 every 4 weeks for up to 144 weeks.

Arm type	Experimental
Investigational medicinal product name	DAC HYP 150 mg SC injection every 4 weeks
Investigational medicinal product code	Daclizumab High Yield Process
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Daclizumab High Yield Process 150 mg subcutaneous (SC) injection every 4 weeks.

Arm title	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)

Arm description:

DAC HYP 150 mg subcutaneous (SC) injection every 4 weeks for up to 4.6 years in this long-term extension study 205MS303 (303); includes subjects who previously received DAC HYP 150 mg SC injection in Study 205MS301 (301) every 4 weeks for up to 144 weeks.

Arm type	Experimental
Investigational medicinal product name	DAC HYP 150 mg SC injection every 4 weeks
Investigational medicinal product code	Daclizumab High Yield Process
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Daclizumab High Yield Process 150 mg subcutaneous (SC) injection every 4 weeks.

Arm title	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)

Arm description:

DAC HYP 150 mg SC injection every 4 weeks for up to 93.7 weeks in this long-term extension study 303 (subjects started at Week 144 of the study); includes subjects who previously received DAC HYP 150 mg SC injection in study 205MS302 (302) every 4 weeks for up to 24 weeks followed by a 20-week washout period then continued treatment for up to an additional 3 years.

Arm type	Experimental
Investigational medicinal product name	DAC HYP 150 mg SC injection every 4 weeks
Investigational medicinal product code	Daclizumab High Yield Process
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Daclizumab High Yield Process 150 mg subcutaneous (SC) injection every 4 weeks.

Arm title	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)

Arm description:

DAC HYP 150 mg SC injection every 4 weeks for up to 94. 1 weeks in this long-term extension study 303 (subjects started at Week 144 of the study); includes subjects who previously received DAC HYP 150 mg SC injection in study 205MS203 (203) every 4 weeks for up to 288 weeks.

Arm type	Experimental
Investigational medicinal product name	DAC HYP 150 mg SC injection every 4 weeks
Investigational medicinal product code	Daclizumab High Yield Process
Other name	
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Daclizumab High Yield Process 150 mg subcutaneous (SC) injection every 4 weeks.

Number of subjects in period 1[1]	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)
Started	597	606	70
Completed	48	38	62
Not completed	549	568	8
Adverse event, non-fatal	104	128	4
Death	2	4	-
Reason Not Specified	280	295	-
Investigator decision	21	15	-
Lost to follow-up	9	8	1
Consent withdrawn	130	117	3
Disease progression, defined by protocol	3	1	-

Number of subjects in period 1[1]	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Started	227
Completed	154
Not completed	73
Adverse event, non-fatal	21
Death	-
Reason Not Specified	15
Investigator decision	-
Lost to follow-up	2
Consent withdrawn	35
Disease progression, defined by protocol	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One subject who had an adverse event and did not receive study drug is not included.

Baseline characteristics

Reporting groups	
Reporting group title	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)
Reporting group description:	
Daclizumab High Yield Process (DAC HYP) 150 mg SC injection every 4 weeks for up to 4.6 years in this long-term extension study 303; includes subjects who previously received interferon beta-1a (IFN β-1a) 30 µg intramuscular (IM) injection once weekly in study 301 every 4 weeks for up to 144 weeks.	
Reporting group title	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Reporting group description:	
DAC HYP 150 mg subcutaneous (SC) injection every 4 weeks for up to 4.6 years in this long-term extension study 205MS303 (303); includes subjects who previously received DAC HYP 150 mg SC injection in Study 205MS301 (301) every 4 weeks for up to 144 weeks.	
Reporting group title	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)
Reporting group description:	
DAC HYP 150 mg SC injection every 4 weeks for up to 93.7 weeks in this long-term extension study 303 (subjects started at Week 144 of the study); includes subjects who previously received DAC HYP 150 mg SC injection in study 205MS302 (302) every 4 weeks for up to 24 weeks followed by a 20-week washout period then continued treatment for up to an additional 3 years.	
Reporting group title	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Reporting group description:	
DAC HYP 150 mg SC injection every 4 weeks for up to 94. 1 weeks in this long-term extension study 303 (subjects started at Week 144 of the study); includes subjects who previously received DAC HYP 150 mg SC injection in study 205MS203 (203) every 4 weeks for up to 288 weeks.	

Reporting group values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)
Number of subjects	597	606	70
Age, Customized Units: Subjects			
Adults (18-64 years)	597	606	70
Sex: Female, Male Units: Subjects			
Female	394	400	42
Male	203	206	28
Race/Ethnicity, Customized Units: Subjects			
White|	546	559	2
Black or African American|	5	5	3
Asian|	11	10	0
Other|	18	14	1
Not Reported|	17	18	64
Age Units: Subjects			
adullt	597	606	70

Reporting group values	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)	Total	
Number of subjects	227	1500	

Age, Customized Units: Subjects			
Adults (18-64 years)	227	1500	
Sex: Female, Male Units: Subjects			
Female	130	966	
Male	97	534	
Race/Ethnicity, Customized Units: Subjects			
White|	223	1330	
Black or African American|	0	13	
Asian|	4	25	
Other|	0	33	
Not Reported|	0	99	
Age Units: Subjects			
adullt	227	1500	

Subject analysis sets

Subject analysis set title	DAC HYP 150 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received DAC HYP 150 mg SC injection in study 205MS303.

Reporting group values	DAC HYP 150 mg		
Number of subjects	1500		
Age, Customized Units: Subjects			
Adults (18-64 years)	1500		
Sex: Female, Male Units: Subjects			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
White|			
Black or African American|			
Asian|			
Other|			
Not Reported|			
Age Units: Subjects			
adullt			

End points

End points reporting groups

Reporting group title	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)

Reporting group description:

Daclizumab High Yield Process (DAC HYP) 150 mg SC injection every 4 weeks for up to 4.6 years in this long-term extension study 303; includes subjects who previously received interferon beta-1a (IFN β-1a) 30 µg intramuscular (IM) injection once weekly in study 301 every 4 weeks for up to 144 weeks.

Reporting group title	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)

Reporting group description:

DAC HYP 150 mg subcutaneous (SC) injection every 4 weeks for up to 4.6 years in this long-term extension study 205MS303 (303); includes subjects who previously received DAC HYP 150 mg SC injection in Study 205MS301 (301) every 4 weeks for up to 144 weeks.

Reporting group title	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)

Reporting group description:

DAC HYP 150 mg SC injection every 4 weeks for up to 93.7 weeks in this long-term extension study 303 (subjects started at Week 144 of the study); includes subjects who previously received DAC HYP 150 mg SC injection in study 205MS302 (302) every 4 weeks for up to 24 weeks followed by a 20-week washout period then continued treatment for up to an additional 3 years.

Reporting group title	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)

Reporting group description:

DAC HYP 150 mg SC injection every 4 weeks for up to 94. 1 weeks in this long-term extension study 303 (subjects started at Week 144 of the study); includes subjects who previously received DAC HYP 150 mg SC injection in study 205MS203 (203) every 4 weeks for up to 288 weeks.

Subject analysis set title	DAC HYP 150 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received DAC HYP 150 mg SC injection in study 205MS303.

Primary: Number of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects with Adverse Events (AEs) and Serious Adverse Events (SAEs)[1]

End point description:

An AE is defined as any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product; it does not necessarily have to have a causal relationship with this treatment. An AE could therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product. An SAE is any untoward medical occurrence or effect that at any dose results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability / incapacity, is a congenital anomaly / birth defect or is medically important due to other reasons than the above mentioned criteria. Safety Population consisted of all subjects who completed Study 301, 203 or 302 and had at least 1 dose of DAC HYP during Study 303.

End point type	Primary

End point timeframe:

First dose of study drug in Study 303 to within 180 days of last dose (up to approximately 5.5 years)

Notes:

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

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: subjects				
Subjects with AEs	541	560	53	172
Subjects with SAEs	157	190	15	38

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Relapse Rate (ARR) in the 205MS303 Treatment Period

End point title	Annualized Relapse Rate (ARR) in the 205MS303 Treatment Period

End point description:

Relapses are defined as new or recurrent neurological symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurological findings upon examination by the Study Neurologist. The unadjusted ARR was calculated by tabulating the total number of relapses experienced in the group divided by the number of days up to the end of study, and the ratio then multiplied by 365.25. Relapses that occurred after subjects received alternative multiple sclerosis (MS) medications were excluded from the analyses. ARR was adjusted for relapse rate, IFN beta use, Expanded Disability Status Scale (EDSS) (<=2.5 vs >2.5) and age (<=35 vs >35) prior to start of study treatment in 205MS301, calculated using the negative binomial model. Intent-to-treat (ITT) Population consisted of all subjects who completed Study 301, 203 or 302 and received at least 1 dose of DAC HYP during Study 303.

End point type	Secondary

End point timeframe:

Up to 4.6 years in the 303 study

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: relapses per year				
arithmetic mean (confidence interval 95%)	0.158 (0.134 to 0.188)	0.163 (0.138 to 0.193)	0.167 (0.097 to 0.288)	0.080 (0.047 to 0.136)

Statistical analyses

No statistical analyses for this end point

Secondary: ARR in the 205MS301-303 Combined Study Period and 205MS301 Treatment Period

End point title	ARR in the 205MS301-303 Combined Study Period and

	205MS301 Treatment Period[2]

End point description:

Relapses are defined as new or recurrent neurological symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurological findings upon examination by the Study Neurologist. The unadjusted ARR was calculated by tabulating the total number of relapses experienced in the group divided by the number of days up to the end of study, and the ratio then multiplied by 365.25. Relapses that occurred after subjects received alternative MS medications were excluded from the analyses. ARR was adjusted for relapse rate, IFN beta use, EDSS (<=2.5 vs >2.5) and age (<=35 vs >35) prior to start of study treatment in 301, calculated using the negative binomial model. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least 1 dose of DAC HYP during Study 303.

End point type	Secondary

End point timeframe:

Up to 5.6 years combining 303 with the initial Study 301; Up to 1 year in the 301 study

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: relapses per year				
arithmetic mean (confidence interval 95%)				
301-303 Combined Study Period	0.247 (0.220 to 0.279)	0.175 (0.154 to 0.199)		
301 Treatment Period	0.317 (0.280 to 0.360)	0.195 (0.169 to 0.225)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Relapse in the 205MS303 Treatment Period

End point title	Number of Subjects with Relapse in the 205MS303 Treatment Period

End point description:

Relapses are defined as new or recurrent neurological symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurological findings upon examination by the Study Neurologist. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and had at least 1 dose of DAC HYP during Study 303.

End point type	Secondary

End point timeframe:

Up to 4.6 years in the 303 study

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: subjects	184	172	16	35

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Relapse in the 205MS301-303 Combined Study Period

End point title	Number of Subjects with Relapse in the 205MS301-303 Combined Study Period[3]

End point description:

Relapses are defined as new or recurrent neurological symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurological findings upon examination by the Study Neurologist. 301-303 ITT Population consisted of all subjects who completed Study 301 and had at least 1 dose of DAC HYP during Study 303.

End point type	Secondary

End point timeframe:

Up to 5.6 years combining 303 with the initial Study 301

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects	339	261		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Sustained Disability Progression in the 205MS303 Treatment Period

End point title	Number of Subjects with Sustained Disability Progression in the 205MS303 Treatment Period

End point description:

Sustained disability progression is defined as at least a 1.0-point increase on the Expanded Disability Status Scale (EDSS) from 303 baseline EDSS ≥1.0 that is sustained for 24 weeks, or at least a 1.5-point increase on the EDSS from 303 baseline EDSS of 0, that is sustained for 24 weeks. The EDSS measures the disability status of people with multiple sclerosis on a scale that ranges from 0 to 10. The range of main categories include (0) =normal neurologic exam; to (5) = ambulatory without aid or rest for 200 meters; disability severe enough to impair full daily activities; to (10) = death due to MS. Higher scores

indicate more disability. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and had at least 1 dose of DAC HYP during Study 303.

End point type	Secondary

End point timeframe:

Up to 4.6 years in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: subjects	95	97	2	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Sustained Disability Progression in the 205MS301-303 Combined Study Period

End point title	Number of Subjects with Sustained Disability Progression in the 205MS301-303 Combined Study Period[4]

End point description:

Sustained disability progression is defined as at least a 1.0-point increase on the Expanded Disability Status Scale (EDSS) from 303 baseline EDSS ≥1.0 that is sustained for 24 weeks, or at least a 1.5-point increase on the EDSS from 303 baseline EDSS of 0, that is sustained for 24 weeks. The EDSS measures the disability status of people with multiple sclerosis on a scale that ranges from 0 to 10. The range of main categories include (0) =normal neurologic exam; to (5) = ambulatory without aid or rest for 200 meters; disability severe enough to impair full daily activities; to (10) = death due to MS. Higher scores indicate more disability. 301-303 ITT Population consisted of all subjects who completed Study 301 and had at least 1 dose of DAC HYP during Study 303.

End point type	Secondary

End point timeframe:

Up to 5.6 years combining 303 with the initial Study 301

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects	144	130		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with New or Newly Enlarging T2 Hyperintense Lesions in the 205MS303 Treatment Period

End point title	Number of Subjects with New or Newly Enlarging T2 Hyperintense Lesions in the 205MS303 Treatment Period[5]

End point description:

T2 Hyperintense Lesions were assessed by magnetic resonance imaging (MRI) and were analysed by a central MRI reader. The number of subjects with New or Newly Enlarging T2 Hyperintense Lesions relative to the 303 Baseline in the 303 Treatment Period is reported. 301-303 ITT population consisted of all subjects who completed Study 301 and received at least 1 dose of DAC HYP during Study 303. No data was collected for subjects from the 203 and 302 studies. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 48, 96, 144, 192, 240 in Study 303

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects				
Week 48 (n= 530, 499)	270	144		
Week 96 (n= 376, 345)	213	130		
Week 144 (n= 375, 370)	223	157		
Week 192 (n= 261, 267)	173	126		
Week 240 (n= 37, 45)	20	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with New or Newly Enlarging T2 Hyperintense Lesions in the 205MS301 Treatment Period

End point title	Number of Subjects with New or Newly Enlarging T2 Hyperintense Lesions in the 205MS301 Treatment Period[6]

End point description:

T2 Hyperintense Lesions were assessed by MRI and were analysed by a central MRI reader. The number of subjects with New or Newly Enlarging T2 Hyperintense Lesions relative to the 301 Baseline in the 301 Treatment Period is reported. 301-303 ITT population consisted of all subjects who completed Study 301 and received at least 1 dose of DAC HYP during Study 303. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 301, Weeks 24, 96, 144 in Study 301

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects				
Week 24 (n= 586, 595)	347	314		
Week 96 (n= 587, 590)	435	368		
Week 144 (n= 167, 165)	126	113		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Gadolinium-enhancing (Gd+) Lesions in the 205MS303 Treatment Period

End point title	Number of Subjects with Gadolinium-enhancing (Gd+) Lesions in the 205MS303 Treatment Period

End point description:

Gd+ lesions were evaluated by MRI and were analysed by a central MRI reader. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAY HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no subjects were analysed.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 48, 96, 144, 192, 240; 203-303 and 302-303: Week 96

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: subjects				
Baseline 303 (n= 591, 590, 0, 0)	180	77	999999	999999
Week 48 (n= 533, 510, 0, 0)	89	46	999999	999999
Week 96 (n= 375, 353, 147, 52)	43	23	2	8
Week 144 (n= 375, 374, 0, 0)	43	42	999999	999999
Week 192 (n= 261, 272, 0, 0)	25	29	999999	999999
Week 240 (n= 37, 44, 0, 0)	1	7	999999	999999

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Gadolinium-enhancing (Gd+) Lesions in the 205MS301 Treatment Period

End point title	Number of Subjects with Gadolinium-enhancing (Gd+) Lesions in the 205MS301 Treatment Period[7]

End point description:

Gd+ lesions were evaluated by MRI and were analysed by a central MRI reader. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least one dose of DAY HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 301, Weeks 24, 96 and 144

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects				
Baseline 301 (n= 591, 595)	263	265		
Week 24 (n= 593, 604)	153	119		
Week 96 (n= 593, 598)	172	66		
Week 144 (n= 168, 167)	49	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with New T1 Hypointense Lesions in the 205MS303 Treatment Period

End point title	Number of Subjects with New T1 Hypointense Lesions in the 205MS303 Treatment Period[8]

End point description:

T1 hypointense lesions were evaluated by MRI and were analysed by a central MRI reader. The number of subjects with New T1 Hyperintense Lesions relative to the 303 Baseline in the 303 Treatment Period is reported. 301-303 ITT Population consisted of all subjects who completed Study 303 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 48, 96, 144, 192, 240 in Study 303

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects				
Week 48 (n= 531, 510)	200	96		
Week 96 (n= 376, 352)	168	91		
Week 144 (n= 375, 374)	184	116		
Week 192 (n= 261, 272)	152	94		
Week 240 (n= 37, 44)	16	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with New T1 Hypointense Lesions in the 205MS301 Treatment Period

End point title	Number of Subjects with New T1 Hypointense Lesions in the 205MS301 Treatment Period[9]

End point description:

T1 hypointense lesions were evaluated by MRI and were analysed by a central MRI reader. The number of subjects with New T1 Hyperintense Lesions relative to the 301 Baseline in the 301 Treatment Period is reported. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least 1 dose of DAC HYP during Study 303. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 301, Weeks 24, 96, 144 in Study 301

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects				
Week 24 (n= 585, 594)	276	244		
Week 96 (n= 584, 588)	375	300		
Week 144 (n= 166, 164)	111	87		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Brain Volume from the 205MS303 Baseline

End point title	Percent Change in Brain Volume from the 205MS303

End point description:

To assess brain atrophy, total brain volume was measured by MRI and was analysed by a central MRI reader. A negative percent change from baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed Study 303 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. No data was collected for subjects from the 203 and 302 studies.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 48, 96, 144, 192, 240 in Study 303

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: percent change				
arithmetic mean (standard deviation)				
Week 48 (n= 400, 360)	-0.451 (± 0.5917)	-0.355 (± 0.5100)		
Week 96 (n= 293, 280)	-0.713 (± 0.7288)	-0.549 (± 0.6126)		
Week 144 (n= 290, 287)	-1.050 (± 0.8566)	-0.801 (± 0.7145)		
Week 192 (n= 216, 222)	-1.225 (± 1.0139)	-0.967 (± 0.8772)		
Week 240 (n= 30, 41)	-1.261 (± 1.0382)	-0.852 (± 0.9890)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Brain Volume from 205MS301 Baseline

End point title	Percent Change in Brain Volume from 205MS301 Baseline[11]

End point description:

To assess brain atrophy, total brain volume was measured by MRI and was analysed by a central MRI reader. A negative percent change from baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed Study 303 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 301, Weeks 48, 96, 144, 192, 240 in Study 303

Notes:

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

Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: percent change				
arithmetic mean (standard deviation)				
Week 48 (n= 462, 427)	-1.535 (± 1.1975)	-1.409 (± 1.1538)		
Week 96 (n= 338, 315)	-1.871 (± 1.3720)	-1.595 (± 1.0736)		
Week 144 (n= 333, 333)	-2.165 (± 1.4596)	-1.812 (± 1.2044)		
Week 192 (n= 258, 261)	-2.403 (± 1.6088)	-1.970 (± 1.3439)		
Week 240 (n= 36, 44)	-2.415 (± 1.6005)	-1.922 (± 1.2258)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Volume of T2 Hyperintense Lesions in the 205MS303 Treatment Period

End point title	Total Volume of T2 Hyperintense Lesions in the 205MS303 Treatment Period

End point description:

Volume of T2 hyperintense Lesions was evaluated by MRI and was analysed by a central MRI reader. ITT Population included all subjects who completed Study 301, 203 or 302 and received at least 1 dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no subjects were analysed.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 48, 96, 144, 192, 240 in Study 303; 203-303 and 302-303: Week 96

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: millimeters cubed (mm^3)				
arithmetic mean (standard deviation)				
Baseline 303 (n= 593, 592, 0, 0)	10357.54 (± 11977.864)	9323.33 (± 10777.863)	999999 (± 999999)	999999 (± 999999)
Week 48 (n= 530, 499, 0, 0)	10738.32 (± 12358.857)	9524.23 (± 10822.502)	999999 (± 999999)	999999 (± 999999)

Week 96 (n= 376, 345, 147, 53)	11498.94 (± 12769.813)	10018.09 (± 11432.768)	12627.51 (± 14777.178)	16116.01 (± 16791.388)
Week 144 (n= 375, 370, 0, 0)	11242.79 (± 12838.060)	10265.04 (± 11324.227)	999999 (± 999999)	999999 (± 9999999)
Week 192 (n= 261, 267, 0, 0)	12453.96 (± 13643.373)	10662.66 (± 11815.075)	999999 (± 999999)	999999 (± 999999)
Week 240 (n= 37, 45, 0, 0)	9368.05 (± 12428.209)	9230.78 (± 11395.493)	99999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Multiple Sclerosis Functional Composite (MSFC) Score in the 205MS303 Treatment Period

End point title	Change from Baseline in the Multiple Sclerosis Functional Composite (MSFC) Score in the 205MS303 Treatment Period[12]

End point description:

MSFC is a three-part, standardised, quantitative, assessment instrument consisting of (Timed 25-Foot Walk, Nine-Hole Peg Test (9HPT) and Paced Auditory Serial Addition Test (PASAT-3”). 2 timed 25-foot walk scores are averaged. 4 trials of the Peg Test (2 for each hand) are converted to the reciprocals and averaged. The number correct of the PASAT-3 is used. The composite Z-score is calculated by: Z(25-foot walk) + Z (HPT) + Z(PASAT)/3. A positive change from baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. No data was collected from subjects from the 203 and 302 studies.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 12, 24 and 48 in Study 303

Notes:

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

Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: z-score				
median (full range (min-max))				
Baseline 303 (n= 596, 606)	0.24958 (-5.5818 to 1.2110)	0.30019 (-6.1660 to 1.5643)		
Change to Week 12 (n= 584, 583)	0.00010 (-3.3934 to 1.6147)	-0.01021 (-4.5948 to 0.9577)		
Change to Week 24 (n= 564, 554)	-0.00599 (-2.7855 to 1.6913)	-0.00010 (-3.4062 to 1.3673)		
Change to Week 48 (n= 529, 507)	-0.01026 (-3.7220 to 1.7775)	-0.01897 (-3.5941 to 1.4111)		

Statistical analyses

Statistical analysis title	Analysis 1
Statistical analysis description: Change to Week 12	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5937
Method	ANCOVA

Statistical analysis title	Analysis 3
Statistical analysis description: Change to Week 48	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1884
Method	ANCOVA

Statistical analysis title	Analysis 2
Statistical analysis description: Change to Week 24	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6233
Method	ANCOVA

Secondary: Change from 205MS301 Baseline in the MSFC Score in the 205MS301-303 Combined Study Period

End point title	Change from 205MS301 Baseline in the MSFC Score in the 205MS301-303 Combined Study Period[13]

End point description:

MSFC is a three-part, standardised, quantitative, assessment instrument consisting of (Timed 25-Foot Walk, Nine-Hole Peg Test (9HPT) and Paced Auditory Serial Addition Test (PASAT-3”). 2 timed 25-foot walk scores are averaged. 4 trials of the Peg Test (2 for each hand) are converted to the reciprocals and averaged. The number correct of the PASAT-3 is used. The composite Z-score is calculated by: Z(25-foot walk) + Z (HPT) + Z(PASAT)/3. A positive change from baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 301, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156 in the 301 study, Baseline 303, Weeks 12, 24, 48 in the 303 study

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: z-score				
median (full range (min-max))				
Baseline (BL) 301 (n= 596, 605)	0.14629 (-6.4963 to 1.3731)	0.14298 (-2.9163 to 1.3865)		
Change from BL 301 to Week 12 for 301 (n=592, 603)	-0.00133 (-1.8674 to 6.4516)	0.02593 (-1.7953 to 2.3905)		
Change from BL 301 to Week 24 for 301 (n=594, 599)	0.02377 (-1.9966 to 6.2712)	0.04728 (-4.3661 to 2.1389)		
Change from BL 301 to Week 36 for 301 (n=593, 597)	0.04764 (-3.0131 to 6.2565)	0.05771 (-11.0047 to 2.1389)		
Change from BL 301 to Week 48 for 301 (n=592, 601)	0.06491 (-1.6103 to 6.5816)	0.07793 (-1.3713 to 2.1024)		
Change from BL 301 to Week 60 for 301 (n=589, 598)	0.06893 (-4.4756 to 6.6543)	0.08973 (-1.3564 to 1.9165)		
Change from BL 301 to Week 72 for 301 (n=592, 600)	0.08645 (-3.7849 to 6.7127)	0.08690 (-5.6579 to 2.0135)		
Change from BL 301 to Week 84 for 301 (n=591, 597)	0.05704 (-4.3418 to 6.6940)	0.10283 (-5.4012 to 2.0493)		
Change from BL 301 to Week 96 for 301 (n=593, 600)	0.06731 (-4.1506 to 6.8296)	0.11283 (-5.8373 to 2.2536)		
Change from BL 301 to Week 108 for 301(n=489, 500)	0.08020 (-4.8814 to 6.8182)	0.09868 (-5.0171 to 2.4199)		
Change from BL 301 to Week 120 for 301(n=397, 395)	0.08406 (-4.4964 to 6.8441)	0.10367 (-3.4544 to 1.2502)		
Change from BL 301 to Week 132 for 301(n=273, 289)	0.07712 (-4.6292 to 3.6137)	0.08682 (-3.9359 to 3.2500)		

Change from BL 301 to Week 144 for 301(n=210, 203)	0.09674 (-2.1875 to 4.0089)	0.12943 (-0.8767 to 1.2626)		
Change from BL 301 to Week 156 for 301 (n= 0, 1)	999999 (999999 to 999999)	-0.0272 (-0.0272 to -0.0272)		
Change from BL 301 to BL 303 (n= 595, 603)	0.06638 (-1.9364 to 6.8441)	0.11003 (-5.0171 to 3.3811)		
Change from BL 301 to Week 12 for 303 (n=582, 579)	0.06449 (-2.8537 to 6.9351)	0.09616 (-5.3094 to 3.3600)		
Change from BL 301 to Week 24 for 303 (n=562, 550)	0.07140 (-2.7241 to 6.7870)	0.12955 (-5.0936 to 3.2141)		
Change from BL 301 to Week 48 for 303 (n=527, 503)	0.05533 (-2.8215 to 7.0425)	0.09332 (-5.3475 to 3.3180)		

Statistical analyses

Statistical analysis title	Analysis 1
Statistical analysis description: Change from Baseline 301 to Week 12 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0204
Method	ANCOVA

Statistical analysis title	Analysis 2
Statistical analysis description: Change from Baseline 301 to Week 24 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0805
Method	ANCOVA

Statistical analysis title	Analysis 3
Statistical analysis description: Change from Baseline 301 to Week 36 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)

Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2535
Method	ANCOVA

Statistical analysis title	Analysis 4
Statistical analysis description: Change from Baseline 301 to Week 48 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4738
Method	ANCOVA

Statistical analysis title	Analysis 5
Statistical analysis description: Change from Baseline 301 to Week 60 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2302
Method	ANCOVA

Statistical analysis title	Analysis 6
Statistical analysis description: Change from Baseline 301 to Week 72 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8522
Method	ANCOVA

Statistical analysis title	Analysis 7
Statistical analysis description: Change from Baseline 301 to Week 84 for 301	

Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0431
Method	ANCOVA

Statistical analysis title	Analysis 8
Statistical analysis description:	
Change from Baseline 301 to Week 96 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0339
Method	ANCOVA

Statistical analysis title	Analysis 9
Statistical analysis description:	
Change from Baseline 301 to Week 108 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3195
Method	ANCOVA

Statistical analysis title	Analysis 10
Statistical analysis description:	
Change from Baseline 301 to Week 120 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2119
Method	ANCOVA

Statistical analysis title	Analysis 11

Statistical analysis description:	
Change from Baseline 301 to Week 132 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3619
Method	ANCOVA

Statistical analysis title	Analysis 12
Statistical analysis description:	
Change from Baseline 301 to Week 144 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	ANCOVA

Statistical analysis title	Analysis 13
Statistical analysis description:	
Change from Baseline 301 to Baseline 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	ANCOVA

Statistical analysis title	Analysis 14
Statistical analysis description:	
Change from Baseline 301 to Week 12 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0849
Method	ANCOVA

Statistical analysis title	Analysis 15
Statistical analysis description: Change from Baseline 301 to Week 24 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0057
Method	ANCOVA

Statistical analysis title	Analysis 16
Statistical analysis description: Change from Baseline 301 to Week 48 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.396
Method	ANCOVA

Secondary: Change from Baseline in the Expanded Disability Status Scale (EDSS) Score in the 205MS303 Treatment Period

End point title	Change from Baseline in the Expanded Disability Status Scale (EDSS) Score in the 205MS303 Treatment Period

End point description:

The EDSS measures the disability status of people with multiple sclerosis as assessed by the Study Neurologist based on 8 functional systems that ranges from 0=normal neurologic exam; to 5=ambulatory without aid or rest for 200 meters; disability severe enough to impair full daily activities; to 10=death due to MS. Higher scores indicate more disability. A negative change from Baseline indicates improvement. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no subjects were analysed.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240, 260; 203-303 and 302-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 116 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: score on a scale				
arithmetic mean (standard deviation)				

Baseline 303 (n= 595, 605, 226, 70)	2.50 (± 1.468)	2.44 (± 1.409)	2.56 (± 1.395)	2.86 (± 1.500)
Change at Week 12 (n= 586, 592, 7, 2)	0.04 (± 0.464)	0.02 (± 0.467)	0.00 (± 0.000)	0.14 (± 0.244)
Change at Week 24 (n= 585, 581, 223, 70)	0.06 (± 0.570)	0.03 (± 0.480)	-0.06 (± 0.325)	0.02 (± 0.237)
Change at Week 48 (n= 551, 541, 215, 69)	0.09 (± 0.614)	0.06 (± 0.495)	-0.05 (± 0.455)	0.00 (± 0.349)
Change at Week 72 (n= 520, 495, 204, 64)	0.11 (± 0.670)	0.10 (± 0.548)	0.00 (± 0.542)	0.04 (± 0.378)
Change at Week 96 (n= 492, 469, 193, 55)	0.13 (± 0.729)	0.13 (± 0.602)	0.01 (± 0.486)	0.04 (± 0.400)
Change at Week 116 (n= 0, 0, 150, 54)	999999 (± 999999)	999999 (± 999999)	0.11 (± 0.572)	0.05 (± 0.353)
Change at Week 120 (n= 453, 441, 0, 0)	0.17 (± 0.768)	0.11 (± 0.578)	999999 (± 99999)	999999 (± 999999)
Change at Week 144 (n= 426, 417, 0, 0)	0.16 (± 0.742)	0.17 (± 0.701)	999999 (± 999999)	999999 (± 999999)
Change at Week 168 (n= 393, 381, 0, 0)	0.22 (± 0.798)	0.19 (± 0.765)	999999 (± 999999)	999999 (± 999999)
Change at Week 192 (n= 344, 348, 0, 0)	0.22 (± 0.756)	0.22 (± 0.777)	999999 (± 999999)	999999 (± 999999)
Change at Week 216 (n= 307, 315, 0, 0)	0.22 (± 0.775)	0.22 (± 0.762)	999999 (± 999999)	999999 (± 999999)
Change at Week 240 (n= 224, 223, 0, 0)	0.19 (± 0.789)	0.26 (± 0.829)	999999 (± 999999)	999999 (± 999999)
Change at Week 260 (n= 18, 12, 0, 0)	0.53 (± 1.007)	-0.17 (± 0.718)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Are Free from Disease Activity in the 205MS303 Treatment Period

End point title	Number of Subjects Who Are Free from Disease Activity in the 205MS303 Treatment Period[14]

End point description:

Subjects without clinical or radiological activity are defined as disease-free. Clinical activity includes assessment of relapses and of disease progression. Radiological activity includes assessments of Gd+ lesions and new or enlarging T2 lesions. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least 1 dose of DAC HYP during Study 303. No data was collected for subjects from the 203 and 302 studies.

End point type	Secondary

End point timeframe:

Up to 4.6 years in Study 303

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects	9	7		

Statistical analyses

Statistical analysis title	Analysis 1
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8417
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.902
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.329
upper limit	2.473

Secondary: Change from Baseline in the Multiple Sclerosis Impact Scale 29 (MSIS 29) Physical and Psychological Scores in the 205MS303 Treatment Period

End point title	Change from Baseline in the Multiple Sclerosis Impact Scale 29 (MSIS 29) Physical and Psychological Scores in the 205MS303 Treatment Period[15]

End point description:

The 29-item MSIS-29 is a disease specific subject-reported outcome measure that has been developed and validated to examine the physical (coordination and mobility) and psychological (mental) impact of MS from a subject's perspective; it measures 20 physical items and 9 psychological items. The results for each of the physical and psychological scores are transformed to a score of 0 to 100 (worse state of health). A negative change from Baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least 1 dose of DAC HYP during Study 303. 'n' is the number of subjects with data available at the given timepoint. No data was collected for subjects from the 203 and 302 studies.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 12, 24, 48, 96, 120 and 144

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: score on a scale				
arithmetic mean (standard deviation)				
Physical Scores: Baseline 303	20.61 (± 20.134)	19.19 (± 19.390)		
Physical Scores: Change to Week 12 (n= 596, 600)	0.22 (± 11.114)	-0.28 (± 9.217)		
Physical Scores: Change to Week 24 (n= 581, 574)	-0.46 (± 10.313)	-0.88 (± 9.147)		
Physical Scores: Change to Week 48 (n=554, 531)	0.12 (± 11.178)	0.13 (± 9.779)		
Physical Scores: Change to Week 96 (n= 173, 165)	2.23 (± 12.713)	0.48 (± 10.617)		
Physical Scores: Change to Week 120 (n= 27, 26)	0.51 (± 9.062)	1.44 (± 10.504)		
Physical Scores: Change to Week 144 (n= 1, 1)	-1.25 (± 0)	-5.00 (± 0)		
Psychological (Psy) Scores: Baseline 303	23.46 (± 21.310)	22.37 (± 20.816)		
Psy Scores: Change to Week 12 (n= 596, 600)	-1.06 (± 12.501)	-0.34 (± 11.226)		
Psy Scores: Change to Week 24 (n= 581, 574)	-1.14 (± 14.154)	-1.69 (± 11.576)		
Psy Scores: Change to Week 48 (n= 554, 531)	-0.46 (± 14.865)	0.10 (± 13.648)		
Psy Scores: Change to Week 96 (n= 173, 165)	-0.16 (± 13.923)	-0.89 (± 14.411)		
Psy Scores: Change to Week 120 (n= 27, 26)	-2.26 (± 10.105)	0.00 (± 8.642)		
Psy Scores: Change to Week 144 (n= 1, 1)	8.33 (± 0)	-13.89 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quality of Life as Assessed by the European Quality of Life, 5 Dimensions (EQ 5D) Health Scores in the 205MS303 Treatment Period

End point title	Change from Baseline in Quality of Life as Assessed by the European Quality of Life, 5 Dimensions (EQ 5D) Health Scores in the 205MS303 Treatment Period

End point description:

The EQ-5D is a self-administered questionnaire consisting of 5 domains pertaining to specific health state profile: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The subjects recorded their level of current health for each domain where: 1=no problems, 2=some problem and 3=severe problems. The health score is derived from the individual scores for each of the 5 domains transformed to a score of 0=worst health state to 1=perfect health state. A positive change from Baseline indicates improvement. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 96, 120, 144, 192, 240; 203-303 and 302-303: Baseline 303, Weeks 48 and 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline 303	0.77 (± 0.233)	0.79 (± 0.201)	0.77 (± 0.213)	0.71 (± 0.242)
Change to Week 12 (n= 596, 600, 0, 0)	0.01 (± 0.168)	-0.01 (± 0.137)	999999 (± 999999)	999999 (± 999999)
Change to Week 24 (n= 581, 574, 0, 0)	0.01 (± 0.171)	0.00 (± 0.144)	999999 (± 999999)	999999 (± 999999)
Change to Week 48 (n= 553, 531, 225, 70)	-0.01 (± 0.185)	-0.01 (± 0.152)	0.00 (± 0.174)	0.00 (± 0.164)
Change to Week 96 (n= 497, 472, 194, 56)	0.00 (± 0.168)	-0.02 (± 0.170)	0.00 (± 0.184)	-0.01 (± 0.162)
Change to Week 120 (n= 448, 431, 0, 0)	0.01 (± 0.166)	-0.01 (± 0.175)	999999 (± 999999)	999999 (± 999999)
Change to Week 144 (n= 416, 409, 0, 0)	0.01 (± 0.187)	-0.02 (± 0.172)	999999 (± 999999)	999999 (± 999999)
Change to Week 192 (n= 332, 338, 0, 0)	0.00 (± 0.187)	-0.03 (± 0.174)	999999 (± 999999)	999999 (± 999999)
Change to Week 240 (n= 103, 105, 0, 0)	-0.01 (± 0.154)	-0.06 (± 0.187)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Quality of Life as Assessed by the European Quality of Life, Visual Analog Scale (EQ VAS) in the 205MS303 Treatment Period

End point title	Change from Baseline in Quality of Life as Assessed by the European Quality of Life, Visual Analog Scale (EQ VAS) in the 205MS303 Treatment Period

End point description:

The subject rated their current health state using the EQ VAS 20-centimeter horizontal line from 0 (worst imaginable health state) to 100 (best imaginable health state). A positive change from baseline indicates improvement. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 96, 120, 44, 192, 240; 203-303 and 302-303: Baseline 303, Weeks 48 and 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline 303	76.19 (± 19.534)	77.74 (± 19.144)	76.97 (± 19.225)	72.13 (± 21.154)
Change at Week 12 (n= 595, 598, 0, 0)	1.42 (± 12.753)	0.25 (± 12.358)	999999 (± 999999)	999999 (± 999999)
Change at Week 24 (n= 581, 574, 0, 0)	1.20 (± 12.135)	0.74 (± 11.400)	999999 (± 999999)	999999 (± 999999)
Change at Week 48 (n= 554, 531, 222, 70)	0.66 (± 12.966)	-0.35 (± 13.543)	-0.64 (± 13.440)	-1.50 (± 13.604)
Change at Week 96 (n= 497, 472, 190, 56)	-0.54 (± 14.963)	0.56 (± 12.054)	-0.95 (± 11.222)	0.45 (± 11.724)
Change at Week 120 (n= 448, 430, 0, 0)	0.80 (± 13.406)	1.52 (± 13.492)	999999 (± 999999)	999999 (± 999999)
Change at Week 144 (n= 416, 409, 0, 0)	0.36 (± 14.263)	1.64 (± 13.648)	999999 (± 999999)	999999 (± 999999)
Change at Week 192 (n= 332, 338, 0, 0)	0.45 (± 15.058)	0.66 (± 14.921)	999999 (± 999999)	999999 (± 999999)
Change at Week 240 (n= 103, 105, 0, 0)	-0.64 (± 11.318)	-1.53 (± 13.082)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: Direct Health Resource Utilisation (HRU): Number of Unscheduled Site Visits in the 205MS303 Treatment Period

End point title	Direct Health Resource Utilisation (HRU): Number of Unscheduled Site Visits in the 205MS303 Treatment Period

End point description:

Heath resource utilisation was assessed by the number of hospitalisations, emergency room visits, and unscheduled neurologist visits for MS-related and non-MS-related visits. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 24, 48, 96, 144, 192, 240; 203-303 and 302-303: Baseline 303, Weeks 48, 96 in 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: site visits				
MS-related: Baseline 303 (n= 557, 549, 201, 67)	141	102	11	27
MS-related: Week 24 (n= 491, 492, 0, 0)	80	48	999999	999999
MS-related: Week 48 (n= 491, 464, 191, 54)	100	70	6	15
MS-related: Week 96 (n= 441, 420, 174, 55)	46	71	3	20
MS-related: Week 144 (n= 396, 378, 0, 0)	37	36	999999	999999
MS-related: Week 192 (n= 321, 319, 0, 0)	26	26	999999	999999
MS-related: Week 240 (n= 119, 128, 0, 0)	6	16	999999	999999
Non-MS related: Baseline 303 (n=557, 549, 201, 67)	90	97	2	15
Non-MS related: Week 24 (n= 491, 492, 0, 0)	81	56	999999	999999
Non-MS related: Week 48 (n= 491, 464, 191, 54)	111	41	5	16
Non-MS related: Week 96 (n= 441, 420, 174, 55)	90	93	10	23
Non-MS related: Week 144 (n= 396, 378, 0, 0)	52	42	999999	999999
Non-MS related: Week 192 (n= 321, 319, 0, 0)	42	39	999999	999999
Non-MS related: Week 240 (n= 119, 128, 0, 0)	10	12	999999	999999

Statistical analyses

No statistical analyses for this end point

Secondary: Direct Health Resource Utilisation (HRU): Number of Unscheduled Site Visits in the 205MS301 Treatment Period

End point title	Direct Health Resource Utilisation (HRU): Number of Unscheduled Site Visits in the 205MS301 Treatment Period[16]

End point description:

Heath resource utilisation was assessed by the number of hospitalisations, emergency room visits, and unscheduled neurologist visits for MS-related and non-MS-related visits. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 301, Weeks 24, 48, 72, 96, 120 and 144 in 301

Notes:

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

Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: site visits				
MS-related: Baseline 301 (n= 446, 440)	277	349		
MS-related: Week 24 (n= 410, 408)	76	78		
MS-related: Week 48 (n= 412, 417)	77	49		
MS-related: Week 72 (n= 411, 413)	60	49		
MS-related: Week 96 (n= 434, 425)	88	53		
MS-related: Week 120 (n= 347, 336)	55	18		
MS-related: Week 144 (n= 184, 186)	13	24		
Non MS-related: Baseline 301 (n= 446, 440)	93	93		
Non MS-related: Week 24 (n= 410, 408)	50	45		
Non MS-related: Week 48 (n= 412, 417)	65	51		
Non MS-related: Week 72 (n= 411, 413)	54	69		
Non MS-relate: Week 96 (n= 434, 425)	44	52		
Non MS-related: Week 120 (n= 347, 336)	43	41		
Non MS-related: Week 144 (n= 184, 186)	24	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Satisfaction as Assessed by the Subject in the 205MS303 Treatment Period

End point title	Treatment Satisfaction as Assessed by the Subject in the 205MS303 Treatment Period[17]

End point description:

Subjects answered the question: "How satisfied or dissatisfied are you with the ability of the medication to prevent or treat the condition?" using the following scale: Dissatisfied (Extremely dissatisfied, Very dissatisfied, Dissatisfied) or Satisfied (Somewhat satisfied, Satisfied, Very Satisfied and Extremely satisfied). The number of subjects in the Dissatisfied and Satisfied categories is reported. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. No data was collected for subjects from the 203 and 302 studies.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 12, 24, 48, 72, 96, 120 in Study 303

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: subjects				
Dissatisfied: Baseline 303 (n= 578, 592)	49	31		
Dissatisfied: Week 12 (n= 586, 584)	46	41		
Dissatisfied: Week 24 (n= 569, 559)	44	27		
Dissatisfied: Week 48 (n= 530, 507)	32	35		
Dissatisfied: Week 72 (n= 503, 472)	27	22		
Dissatisfied: Week 96 (n= 152, 145)	19	9		
Dissatisfied: Week 120 (n= 27, 24)	2	1		
Satisfied: Baseline 303 (n= 578, 592)	529	561		
Satisfied: Week 12 (n= 586, 584)	540	543		
Satisfied: Week 24 (n= 569, 559)	525	532		
Satisfied: Week 48 (n= 530, 507)	498	472		
Satisfied: Week 72 (n= 503, 472)	476	450		
Satisfied: Week 96 (n= 152, 145)	133	136		
Satisfied: Week 120 (n= 27, 24)	25	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Related Productivity Questionnaire (HRPQ): Scheduled Work Hours in the 205MS303 Treatment Period

End point title	Health Related Productivity Questionnaire (HRPQ): Scheduled Work Hours in the 205MS303 Treatment Period

End point description:

The HRPQ was used by the subject to assess the impact of MS or its treatments on employment. The subject recorded their scheduled work hours. Data is reported by part time or full time employment. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicated that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240; 203-303 and 302-303: Baseline 303, Weeks 24, 48, 72, 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: hours				
arithmetic mean (standard deviation)				

Part Time: Baseline 303 (n= 71, 71, 27, 9)	20.4 (± 10.60)	19.5 (± 11.45)	20.2 (± 6.06)	23.6 (± 9.46)
Part Time: Week 12 (n= 71, 69, 0, 0)	21.4 (± 10.30)	22.4 (± 13.62)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 24 (n= 70, 67, 28, 11)	21.2 (± 12.80)	20.6 (± 13.47)	24.5 (± 5.22)	23.5 (± 9.37)
Part Time: Week 48 (n= 67, 68, 24, 11)	22.3 (± 11.12)	21.9 (± 11.28)	27.7 (± 13.79)	22.7 (± 11.23)
Part Time: Week 72 (n= 71, 59, 26, 9)	21.6 (± 12.44)	23.0 (± 11.64)	25.2 (± 6.08)	22.8 (± 11.60)
Part Time: Week 96 (n= 67, 58, 25, 8)	25.7 (± 17.40)	19.9 (± 11.79)	23.5 (± 7.98)	24.8 (± 10.13)
Part Time: Week 120 (n= 54, 49, 0, 0)	27.0 (± 16.13)	20.8 (± 13.15)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 144 (n= 43, 48, 0, 0)	22.9 (± 14.79)	21.4 (± 12.90)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 168 (n= 36, 40, 0, 0)	21.0 (± 12.06)	20.3 (± 11.93)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 192 (n= 35, 36, 0, 0)	23.2 (± 12.07)	23.2 (± 16.37)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 216 (n= 26, 35, 0, 0)	24.9 (± 13.18)	25.3 (± 11.79)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 240 (n= 4, 0, 0, 0)	21.3 (± 8.54)	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)
Full Time: Baseline 303 (n= 288, 301, 114, 41)	36.8 (± 14.23)	37.4 (± 12.71)	40.1 (± 10.44)	39.3 (± 12.23)
Full Time: Week 12 (n= 287, 306, 0, 0)	37.3 (± 14.23)	38.5 (± 18.79)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 24 (n= 278, 287, 115, 39)	35.0 (± 15.43)	36.4 (± 17.43)	42.0 (± 7.34)	37.2 (± 14.19)
Full Time: Week 48 (n= 270, 277, 103, 40)	36.0 (± 13.47)	38.2 (± 20.63)	41.1 (± 8.50)	38.6 (± 10.90)
Full Time: Week 72 (n= 255, 244, 97, 33)	36.9 (± 12.90)	38.5 (± 12.21)	42.0 (± 5.24)	38.4 (± 9.91)
Full Time: Week 96 (n= 235, 232, 92, 33)	36.0 (± 13.42)	37.6 (± 12.35)	41.5 (± 5.05)	36.4 (± 14.36)
Full Time: Week 120 (n= 224, 234, 0, 0)	37.7 (± 11.04)	39.2 (± 22.80)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 144 (n= 219, 210, 0, 0)	37.3 (± 12.79)	39.7 (± 12.68)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 168 (n= 180, 178, 0, 0)	37.3 (± 12.35)	39.4 (± 10.36)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 192 (n= 168, 166, 0, 0)	37.7 (± 10.31)	40.4 (± 9.00)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 216 (n= 155, 152, 0, 0)	37.7 (± 12.44)	38.8 (± 11.68)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 240 (n= 19, 18, 0, 0)	39.8 (± 4.16)	39.3 (± 12.33)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: HRPQ: Number of Subjects where MS or Its Treatments Resulted in Missed Work in the 205MS303 Treatment Period

End point title	HRPQ: Number of Subjects where MS or Its Treatments Resulted in Missed Work in the 205MS303 Treatment Period

End point description:

The HRPQ was used by the subject to assess the impact of MS or its treatments on employment. The subject recorded whether their MS or its treatments caused them to miss work. Data is reported by part time or full time employment. ITT Population consisted of all subjects who completed Study 301, 203 or

302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240; 203-303 and 302-303: Baseline 303, Weeks 24, 48, 72, 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: subjects				
Part Time: Baseline 303 (n= 71, 73, 27, 9)	11	7	1	1
Part Time: Week 12 (n= 73, 69, 0, 0)	10	8	999999	999999
Part Time: Week 24 (n= 70, 67, 28, 11)	12	7	2	3
Part Time: Week 48 (n= 68, 68, 24, 11)	9	7	1	2
Part Time: Week 72 (n= 72, 59, 27, 9)	7	4	2	2
Part Time: Week 96 (n= 68, 58, 25, 8)	6	5	2	2
Part Time: Week 120 (n= 54, 49, 0, 0)	11	6	999999	999999
Part Time: Week 144 (n= 43, 49, 0, 0)	4	6	999999	999999
Part Time: Week 168 (n= 36, 40, 0, 0)	5	6	999999	999999
Part Time: Week 192 (n= 35, 38, 0, 0)	5	3	999999	999999
Part Time: Week 216 (n= 26, 35, 0, 0)	1	4	999999	999999
Part Time: Week 240 (n= 4, 0, 0, 0)	1	999999	999999	999999
Full Time: Baseline 303 (n= 305, 291, 112, 41)	28	30	3	11
Full Time: Week 12 (n= 291, 305, 0, 0)	19	26	999999	999999
Full Time: Week 24 (n= 279, 288, 111, 39)	11	21	3	8
Full Time: Week 48 (n= 271, 277, 104, 40)	20	24	3	6
Full Time: Week 72 (n= 255, 245, 97, 33)	13	10	3	6
Full Time: Week 96 (n= 236, 232, 90, 33)	10	16	1	3
Full Time: Week 120 (n= 224, 235, 0, 0)	8	18	999999	999999
Full Time: Week 144 (n= 219, 210, 0, 0)	16	16	999999	999999
Full Time: Week 168 (n= 182, 178, 0, 0)	10	17	999999	999999
Full Time: Week 192 (n= 170, 166, 0, 0)	10	13	999999	999999
Full Time: Week 216 (n= 155, 152, 0, 0)	6	10	999999	999999
Full Time: Week 240 (n= 19, 18, 0, 0)	0	2	999999	999999

Statistical analyses

No statistical analyses for this end point

Secondary: HRPQ: Hours of Work Missed Due to MS or Its Treatment in the 205MS303 Treatment Period

End point title	HRPQ: Hours of Work Missed Due to MS or Its Treatment in the 205MS303 Treatment Period

End point description:

The HRPQ was used by the subject to assess the impact of MS or its treatments on employment. The subject recorded the hours they missed work due to MS or its treatments. Data is reported by part time or full time employment. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects who missed work with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240; 203-303 and 302-303: Baseline 303, Weeks 24, 48, 72, 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: hours				
arithmetic mean (standard deviation)				
Part Time: Baseline 303 (n= 11, 7, 1, 1)	8.5 (± 5.82)	5.6 (± 4.93)	20.0 (± 0)	12.0 (± 0)
Part Time: Week 12 (n= 12, 8, 0, 0)	8.7 (± 8.43)	8.4 (± 8.11)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 24 (n= 13, 7, 3, 2)	15.2 (± 19.31)	10.1 (± 3.63)	3.0 (± 1.41)	8.3 (± 6.51)
Part Time: Week 48 (n= 9, 7, 2, 1)	8.6 (± 4.85)	12.3 (± 12.83)	15.0 (± 0)	4.5 (± 3.54)
Part Time: Week 72 (n= 6, 4, 2, 2)	7.5 (± 7.01)	10.1 (± 13.05)	7.0 (± 4.24)	16.0 (± 19.80)
Part Time: Week 96 (n= 6, 5, 2, 2)	22.2 (± 38.48)	8.7 (± 12.02)	22.5 (± 3.54)	5.0 (± 0.00)
Part Time: Week 120 (n= 11, 6, 0, 0)	9.5 (± 5.92)	7.3 (± 8.21)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 144 (n= 4, 7, 0, 0)	3.3 (± 2.22)	10.3 (± 7.18)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 168 (n= 5, 6, 0, 0)	7.3 (± 7.90)	5.3 (± 5.16)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 192 (n= 5, 2, 0, 0)	3.6 (± 1.14)	9.0 (± 4.24)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 216 (n= 1, 5, 0, 0)	3.0 (± 0)	16.4 (± 15.71)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 240 (n= 1, 0, 0, 0)	5.0 (± 0)	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)
Full Time: Baseline 303 (n= 26, 30, 11, 3)	11.0 (± 11.42)	15.0 (± 13.58)	8.0 (± 0.00)	8.8 (± 11.39)
Full Time: Week 12 (n= 19, 27, 0, 0)	8.5 (± 10.13)	7.9 (± 8.06)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 24 (n= 13, 23, 8, 3)	11.2 (± 13.80)	12.4 (± 13.31)	7.3 (± 1.15)	14.1 (± 16.27)
Full Time: Week 48 (n= 21, 26, 5, 3)	15.7 (± 15.50)	11.7 (± 11.11)	6.7 (± 3.06)	12.7 (± 15.57)
Full Time: Week 72 (n= 15, 11, 6, 3)	13.8 (± 11.51)	7.6 (± 6.00)	8.7 (± 3.06)	15.0 (± 17.54)
Full Time: Week 96 (n= 11, 17, 3, 1)	14.2 (± 13.19)	16.1 (± 15.14)	3.0 (± 0)	6.7 (± 2.89)
Full Time: Week 120 (n= 10, 20, 0, 0)	12.4 (± 13.88)	10.7 (± 11.19)	999999 (± 999999)	999999 (± 999999)

Full Time: Week 144 (n= 17, 16, 0, 0)	16.0 (± 14.32)	13.1 (± 15.44)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 168 (n= 10, 17, 0, 0)	7.3 (± 4.45)	16.9 (± 15.73)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 192 (n= 10, 13, 0, 0)	15.9 (± 11.94)	10.0 (± 11.53)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 216 (n= 10, 13, 0, 0)	10.3 (± 13.98)	11.2 (± 14.00)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 240 (n= 0, 2, 0, 0)	999999 (± 999999)	14.5 (± 4.95)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: HRPQ: Percent Impact on Employment in the 205MS303 Treatment Period

End point title	HRPQ: Percent Impact on Employment in the 205MS303 Treatment Period

End point description:

The HRPQ was used by the subject to assess the impact of MS or its treatments on employment. The subjects assessed the percent impact of MS and its treatments on their work output using a VAS where 0= MS or its treatments had no impact on how much I accomplished to 100=MS or its treatments kept me from accomplishing anything. Data is reported by part time or full time employment. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240; 203-303 and 302-303: Baseline 303, Weeks 24, 48, 72, 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: percent impact				
arithmetic mean (standard deviation)				
Part Time: Baseline 303 (n= 69, 68, 27, 9)	18.4 (± 24.18)	21.1 (± 26.16)	32.2 (± 34.65)	19.0 (± 24.78)
Part Time: Week 12 (n= 69, 66, 0, 0)	18.8 (± 24.06)	16.0 (± 22.87)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 24 (n= 63, 61, 28, 11)	17.5 (± 24.30)	16.8 (± 22.84)	14.4 (± 14.42)	26.5 (± 33.85)
Part Time: Week 48 (n= 66, 66, 24, 11)	16.0 (± 23.54)	14.0 (± 23.03)	19.1 (± 24.17)	18.8 (± 25.03)
Part Time: Week 72 (n= 70, 58, 27, 9)	20.8 (± 27.63)	18.8 (± 27.93)	11.1 (± 10.83)	23.3 (± 29.50)
Part Time: Week 96 (n= 64, 57, 25, 8)	18.4 (± 24.01)	16.8 (± 23.90)	22.3 (± 33.41)	19.1 (± 23.80)
Part Time: Week 120 (n= 54, 47, 0, 0)	19.6 (± 26.58)	22.4 (± 30.15)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 144 (n= 41, 49, 0, 0)	17.4 (± 23.16)	15.3 (± 24.07)	999999 (± 999999)	999999 (± 999999)

Part Time: Week 168 (n= 35, 39, 0, 0)	35.7 (± 33.82)	15.3 (± 22.93)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 192 (n= 34, 35, 0, 0)	30.9 (± 33.29)	21.4 (± 25.03)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 216 (n= 26, 35, 0, 0)	23.6 (± 27.73)	20.3 (± 28.78)	999999 (± 999999)	999999 (± 999999)
Part Time: Week 240 (n= 4, 0, 0, 0)	7.5 (± 15.00)	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)
Full Time: Baseline 303 (n= 282, 298, 112, 41)	10.0 (± 19.52)	11.8 (± 24.02)	6.7 (± 16.33)	13.9 (± 25.56)
Full Time: Week 12 (n= 288, 301, 0, 0)	8.0 (± 17.72)	10.3 (± 21.17)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 24 (n= 269, 276, 111, 39)	9.1 (± 20.13)	8.3 (± 18.54)	11.2 (± 25.20)	12.7 (± 25.79)
Full Time: Week 48 (n= 258, 271, 103, 40)	8.2 (± 19.37)	9.6 (± 21.75)	9.9 (± 24.25)	12.2 (± 23.87)
Full Time: Week 72 (n= 251, 238, 97, 33)	9.7 (± 21.40)	7.8 (± 18.39)	11.3 (± 22.72)	14.0 (± 23.47)
Full Time: Week 96 (n= 228, 227, 89, 33)	7.3 (± 18.29)	8.4 (± 18.59)	10.2 (± 24.63)	11.1 (± 23.76)
Full Time: Week 120 (n= 223, 230, 0, 0)	6.4 (± 13.87)	8.6 (± 19.19)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 144 (n= 216, 205, 0, 0)	8.2 (± 18.36)	7.8 (± 17.91)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 168 (n= 180, 178, 0, 0)	8.8 (± 18.53)	10.1 (± 22.45)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 192 (n= 167, 166, 0, 0)	9.0 (± 19.23)	7.5 (± 17.59)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 216 (n= 152, 148, 0, 0)	10.0 (± 22.36)	9.3 (± 20.91)	999999 (± 999999)	999999 (± 999999)
Full Time: Week 240 (n= 19, 18, 0, 0)	13.1 (± 23.33)	7.5 (± 18.01)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: HRPQ: Hours of Household Chores Planned to Perform in the 205MS303 Treatment Period

End point title	HRPQ: Hours of Household Chores Planned to Perform in the 205MS303 Treatment Period

End point description:

The HRPQ was used by the subject to assess the impact of MS or its treatments on performing household chores. The subject recorded their planned hours for household chores. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240; 203-303 and 302-303: Baseline 303, Weeks 24, 48, 72, 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: hours				
arithmetic mean (standard deviation)				
Baseline 303 (n= 585, 597, 219, 70)	10.1 (± 10.87)	10.0 (± 10.85)	11.5 (± 7.94)	15.8 (± 13.68)
Week 12 (n= 589, 596, 0, 0)	11.8 (± 11.38)	12.2 (± 12.33)	999999 (± 999999)	999999 (± 999999)
Week 24 (n= 568, 561, 227, 70)	12.0 (± 11.75)	12.6 (± 11.24)	11.1 (± 7.72)	14.4 (± 13.66)
Week 48 (n= 552, 538, 213, 69)	11.6 (± 11.43)	12.6 (± 11.39)	11.6 (± 8.37)	15.7 (± 14.74)
Week 72 (n= 514, 486, 199, 59)	13.3 (± 12.10)	13.9 (± 12.87)	12.3 (± 8.94)	15.0 (± 13.55)
Week 96 (n= 486, 461, 191, 57)	11.9 (± 10.70)	13.5 (± 12.10)	12.6 (± 9.17)	14.8 (± 12.20)
Week 120 (n= 451, 438, 0, 0)	12.6 (± 12.09)	13.1 (± 12.09)	999999 (± 999999)	999999 (± 999999)
Week 144 (n= 426, 412, 0, 0)	13.0 (± 12.89)	13.4 (± 11.99)	999999 (± 999999)	999999 (± 999999)
Week 168 (n= 358, 361, 0, 0)	12.9 (± 12.35)	13.7 (± 12.58)	999999 (± 999999)	999999 (± 999999)
Week 192 (n= 332, 330, 0, 0)	13.4 (± 11.78)	13.9 (± 12.43)	999999 (± 999999)	999999 (± 999999)
Week 216 (n= 292, 299, 0, 0)	14.2 (± 13.01)	14.0 (± 11.46)	999999 (± 999999)	999999 (± 999999)
Week 240 (n= 42, 30, 0, 0)	13.6 (± 11.49)	10.1 (± 7.89)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: HRPQ: Number of Subjects where MS or Its Treatments Kept the Subject from Completing Chores in the 205MS303 Treatment Period

End point title	HRPQ: Number of Subjects where MS or Its Treatments Kept the Subject from Completing Chores in the 205MS303 Treatment Period

End point description:

The HRPQ was used by the subject to assess the impact of MS or its treatments on performing household chores. The subject recorded whether MS or its treatments kept them from completing household chores. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240; 203-303 and 302-303: Baseline 303, Weeks 24, 48, 72, 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: subjects				
Baseline 303 (n= 591, 600, 220, 70)	112	104	15	58
Week 12 (n= 593, 600, 0, 0)	110	111	999999	999999
Week 24 (n= 572, 565, 227, 70)	125	110	12	68
Week 48 (n= 553, 541, 213, 69)	113	93	19	66
Week 72 (n= 515, 489, 199, 59)	111	93	15	58
Week 96 (n= 487, 464, 191, 57)	94	79	16	53
Week 120 (n= 452, 439, 0, 0)	93	84	999999	999999
Week 144 (n= 427, 413, 0, 0)	91	87	999999	999999
Week 168 (n= 359, 362, 0, 0)	82	81	999999	999999
Week 192 (n= 333, 331, 0, 0)	71	65	999999	999999
Week 216 (n= 293, 299, 0, 0)	65	65	999999	999999
Week 240 (n= 42, 30, 0, 0)	2	7	999999	999999

Statistical analyses

No statistical analyses for this end point

Secondary: HRPQ: Hours not Performing Household Chores due to MS or Its Treatment in 205MS303 Treatment Period

End point title	HRPQ: Hours not Performing Household Chores due to MS or Its Treatment in 205MS303 Treatment Period

End point description:

The HRPQ was used by the subject to assess the impact of MS or its treatments on performing household chores. The subject recorded the hours where they were not able to perform household chores due to MS or its treatments. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects unable to complete chores with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240; 203-303 and 302-303: Baseline 303, Weeks 24, 48, 72, 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: hours				
arithmetic mean (standard deviation)				
Baseline 303 (n= 107, 104, 58, 15)	6.4 (± 7.82)	5.1 (± 5.08)	5.2 (± 4.06)	5.4 (± 6.25)
Week 12 (n= 111, 113, 0, 0)	7.0 (± 9.35)	5.9 (± 7.63)	999999 (± 999999)	999999 (± 999999)

Week 24 (n= 124, 109, 67, 12)	6.3 (± 7.56)	5.2 (± 4.59)	5.0 (± 3.57)	5.7 (± 7.75)
Week 48 (n= 111, 89, 66, 19)	7.3 (± 11.41)	4.7 (± 3.53)	4.7 (± 4.21)	7.9 (± 9.19)
Week 72 (n= 110, 94, 59, 15)	7.2 (± 7.16)	6.6 (± 10.32)	5.8 (± 4.46)	6.8 (± 8.03)
Week 96 (n= 95, 77, 53, 17)	5.2 (± 3.93)	5.1 (± 4.67)	3.8 (± 3.81)	8.1 (± 9.35)
Week 120 (n= 92, 84, 0, 0)	6.0 (± 8.23)	5.9 (± 11.13)	999999 (± 999999)	999999 (± 999999)
Week 144 (n= 93, 87, 0, 0)	5.7 (± 4.95)	6.3 (± 6.10)	999999 (± 999999)	999999 (± 999999)
Week 168 (n= 82, 83, 0, 0)	5.8 (± 5.19)	5.5 (± 5.16)	999999 (± 999999)	999999 (± 999999)
Week 192 (n= 72, 65, 0, 0)	6.9 (± 9.01)	5.7 (± 5.96)	999999 (± 999999)	999999 (± 999999)
Week 216 (n= 66, 70, 0, 0)	6.9 (± 7.09)	7.3 (± 10.97)	999999 (± 999999)	999999 (± 999999)
Week 240 (n= 2, 8, 0, 0)	5.5 (± 6.36)	9.8 (± 13.04)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: HRPQ: Percent Impact on Performing Household chores in the 205MS303 Treatment Period

End point title	HRPQ: Percent Impact on Performing Household chores in the 205MS303 Treatment Period

End point description:

The HRPQ was used by the subject to assess the impact of MS or its treatments on performing household chores. The subject assessed the percent impact of MS and its treatments on how much they accomplished using a VAS where 0= MS or its treatments had no impact on how much I accomplished to 100=MS or its treatments kept me from accomplishing anything. ITT Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

301-303: Baseline 303, Weeks 12, 24, 48, 72, 96, 120, 144, 168, 192, 216, 240; 203-303 and 302-303: Baseline 303, Weeks 24, 48, 72, 96 in Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: percent impact				
arithmetic mean (standard deviation)				
Baseline 303 (n= 519, 515, 219, 69)	16.0 (± 23.16)	17.5 (± 25.31)	18.9 (± 24.41)	25.3 (± 29.42)
Week 12 (n= 578, 587, 0, 0)	16.7 (± 24.40)	17.5 (± 25.38)	999999 (± 999999)	999999 (± 999999)
Week 24 (n= 557, 552, 226, 68)	17.0 (± 25.23)	16.7 (± 24.71)	24.8 (± 30.25)	25.5 (± 28.81)
Week 48 (n= 541, 531, 210, 69)	16.9 (± 25.48)	17.1 (± 26.23)	21.0 (± 27.62)	23.8 (± 28.52)
Week 72 (n= 507, 485, 199, 59)	19.9 (± 26.83)	17.8 (± 26.13)	19.6 (± 23.37)	25.4 (± 27.88)

Week 96 (n= 482, 455, 187, 57)	16.4 (± 25.39)	17.7 (± 26.18)	21.4 (± 27.23)	23.8 (± 29.07)
Week 120 (n= 449, 435, 0, 0)	17.4 (± 25.10)	16.9 (± 25.00)	999999 (± 999999)	999999 (± 999999)
Week 144 (n= 421, 411, 0, 0)	16.5 (± 24.40)	17.4 (± 25.25)	999999 (± 999999)	999999 (± 999999)
Week 168 (n= 356, 358, 0, 0)	19.1 (± 26.03)	18.2 (± 26.37)	999999 (± 999999)	999999 (± 999999)
Week 192 (n= 330, 330, 0, 0)	18.5 (± 26.55)	17.3 (± 25.07)	999999 (± 999999)	999999 (± 999999)
Week 216 (n= 291, 298, 0, 0)	18.8 (± 26.11)	18.3 (± 26.18)	999999 (± 999999)	999999 (± 999999)
Week 240 (n= 42, 30, 0, 0)	9.6 (± 14.95)	16.0 (± 26.06)	999999 (± 999999)	999999 (± 999999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Changes from Baseline in Clinical Laboratory Assessments in the 205MS303 Treatment Period

End point title	Number of Subjects with Clinically Significant Changes from Baseline in Clinical Laboratory Assessments in the 205MS303 Treatment Period

End point description:

Clinical Laboratory assessments included tests of hematology, blood chemistry, renal function, and thyroid function. The investigator determined if the results were clinically significant. Safety Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303.

End point type	Secondary

End point timeframe:

Up to 4.6 years Study 303

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	70	227
Units: subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Local Tolerability as assessed by Subject-reported Injection Site Pain VAS

End point title	Local Tolerability as assessed by Subject-reported Injection Site Pain VAS

End point description:

The VAS is a 10 cm-long horizontal line labeled with 2 extremes of pain at either end: 0 =no pain on the left and 100=very painful on the right. The subject rates their perceived pain of each injection by placing a vertical mark on the line to indicate the level of pain. Safety Population included all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects in this study who received DAC HYP with data available for analysis. Local tolerability of the DAC HYP injection was assessed for all subjects who received DAC HYP in Study 303 and is independent of the treatment previously received.

End point type	Secondary

End point timeframe:

After the first and fourth injections in 303, approximately Week 0 and Week 12

End point values	DAC HYP 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	1500			
Units: score on scale				
arithmetic mean (standard deviation)				
First Injection, Post-dose (n= 97)	1.7 (± 2.46)			
Fourth Injection, Post-dose (n=87)	1.6 (± 2.34)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects in Local Tolerability Clinician Injection Site Assessment Categories

End point title	Number of Subjects in Local Tolerability Clinician Injection Site Assessment Categories

End point description:

The investigator assessed the injection site after the first dose and before the fourth dose for the presence of erythema (None, Mild, Moderate, Severe), pigmentation (None, Hypo, Hyper), Induration (None, Mild, Moderate, Severe), Tenderness (None, Mild, Moderate, Severe) and Temperature (Normal, Warm, Hot). The number of subjects in each grade is reported. Safety Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. This outcome measure was assessed for all subjects who received at least one dose of DAC HYP combined. 'n' is the number of subjects with data available at the given timepoint. Local tolerability of the DAC HYP injection was assessed for all subjects who received DAC HYP in Study 303 and is independent of the treatment previously received.

End point type	Secondary

End point timeframe:

After the first and fourth injections in 303, approximately Week 0 and Week 12

End point values	DAC HYP 150 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	1500			
Units: subjects				
First Injection Post-dose, Erythema: None (n= 97)	87			
First Injection Post-dose, Erythema: Mild (n= 97)	8			
First Injection Post-dose,Erythema:Moderate (n=97)	2			
First Injection Post-dose, Erythema: Severe (n=97)	0			
Fourth Injection Pre-dose, Erythema: None (n= 87)	87			
Fourth Injection Pre-dose, Erythema: Mild (n= 87)	0			
Fourth Injection Pre-dose,Erythema:Moderate (n=87)	0			
Fourth Injection Pre-dose, Erythema: Severe (n=87)	0			
First Injection Post-dose,Pigmentation:None (n=97)	90			
First Injection Post-dose,Pigmentation:Hypo (n=97)	7			
First Injection Post-dose,Pigmentation:Hyper(n=97)	0			
Fourth Injection Pre-dose,Pigmentation:None (n=87)	87			
Fourth Injection Pre-dose,Pigmentation:Hypo (n=87)	0			
Fourth Injection Pre-dose,Pigmentation:Hyper(n=87)	0			
First Injection Post-dose, Induration: None (n=93)	89			
First Injection Post-dose, Induration: Mild (n=93)	4			
First Injection Postdose,Induration:Moderate(n=93)	0			
First Injection Post-dose,Induration:Severe (n=93)	0			
Fourth Injection Pre-dose, Induration: None (n=87)	87			
Fourth Injection Pre-dose, Induration: Mild (n=87)	0			
Fourth Injection Predose,Induration:Moderate(n=87)	0			
Fourth Injection Pre-dose,Induration:Severe (n=87)	0			
First Injection Post-dose, Tenderness: None (n=97)	94			
First Injection Post-dose, Tenderness: Mild (n=97)	3			
First Injection Postdose,Tenderness:Moderate(n=97)	0			
First Injection Post-dose,Tenderness:Severe (n=97)	0			
Fourth Injection Pre-dose, Tenderness: None (n=87)	87			
Fourth Injection Pre-dose, Tenderness: Mild (n=87)	0			

Fourth Injection Predose,Tenderness:Moderate(n=87)	0			
Fourth Injection Pre-dose,Tenderness:Severe (n=87)	0			
First Injection Postdose,Temperature:Normal (n=97)	97			
First Injection Post-dose,Temperature:Warm (n=97)	0			
First Injection Post-dose,Temperature: Hot (n= 97)	0			
Fourth Injection Pre-dose,Temperature:Normal(n=87)	87			
Fourth Injection Pre-dose,Temperature:Warm (n=87)	0			
Fourth Injection Pre-dose, Temperature: Hot (n=87)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Anti-BIIB019 Binding Antibodies (ADAbs) in the 205MS303 Treatment Period

End point title	Number of Subjects with Anti-BIIB019 Binding Antibodies (ADAbs) in the 205MS303 Treatment Period

End point description:

Blood samples were collected for ADAbs and were analysed using a laboratory test. The number of subjects ADAb positive at any post-baseline timepoint is reported. Safety Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. Number of subjects analyzed is the number of subjects with evaluable data for this outcome measure.

End point type	Secondary

End point timeframe:

Up to 4.6 years in the 303 Treatment Period

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	603	35	68
Units: subjects	113	48	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Anti-BIIB019 Neutralizing Antibodies (Nabs) in the 205MS303 Treatment Period

End point title	Number of Subjects with Anti-BIIB019 Neutralizing Antibodies

	(Nabs) in the 205MS303 Treatment Period

End point description:

Blood samples were collected for NAbs and were analysed using a laboratory test. The number of subjects NAb positive at any post-baseline timepoint is reported. Safety Population consisted of all subjects who completed Study 301, 203 or 302 and received at least one dose of DAC HYP in Study 303. Number of subjects analyzed is the number of subjects with evaluable data for this outcome measure.

End point type	Secondary

End point timeframe:

Up to 4.6 years in the 303 Treatment Period

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	597	606	35	67
Units: subjects	45	21	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from 205MS303 Baseline in the Symbol Digit Modalities Test (SDMT) Score in the 205MS303 Treatment Period

End point title	Change from 205MS303 Baseline in the Symbol Digit Modalities Test (SDMT) Score in the 205MS303 Treatment Period[18]

End point description:

SDMT is a screening test for cognitive impairment. Subjects are given 90 seconds in which to pair specific numbers with given geometric figures using a key. Scores range from 0 to 110 (best). A positive change from baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least 1 dose of DAC HYP during Study 303. 'n' is the number of subjects with data available at the given timepoint. No data is collected for subjects from 203 and 302 studies.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 144, 168, 192, 240 in 303

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	400		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline 303	52.0 (± 15.13)	52.4 (± 16.08)		

Change at Week 144 (n= 321, 315)	-3.0 (± 11.38)	-3.5 (± 11.91)		
Change at Week 168 (n= 327, 340)	-1.9 (± 11.59)	-3.7 (± 13.10)		
Change at Week 192 (n= 314, 318)	-2.5 (± 12.02)	-2.8 (± 12.92)		
Change at Week 240 (n= 24, 16)	2.0 (± 10.78)	-2.0 (± 15.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from 205MS301 Baseline in the SDMT Score in the 205MS301-303 Combined Study Period

End point title	Change from 205MS301 Baseline in the SDMT Score in the 205MS301-303 Combined Study Period[19]

End point description:

SDMT is a screening test for cognitive impairment. Subjects are given 90 seconds in which to pair specific numbers with given geometric figures using a key. Scores range from 0 to 110 (best). A positive change from baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least one dose of DAC HYP in Study 303. 'n' is the number of subjects with data available at the given timepoint.

End point type	Secondary

End point timeframe:

Baseline 301, Weeks 24, 48, 72, 96, 120, 144 in 301; Weeks 144, 168, 192, 216, 240 in 303

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	577	584		
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (BL) 301	47.8 (± 16.18)	48.4 (± 16.32)		
Change from BL 301 at Week 24 for 301 (n=572, 575)	1.3 (± 11.20)	1.1 (± 12.42)		
Change from BL 301 at Week 48 for 301 (n=568, 577)	2.7 (± 12.31)	2.2 (± 12.01)		
Change from BL 301 at Week 72 for 301 (n=568, 573)	3.0 (± 13.12)	3.6 (± 12.98)		
Change from BL 301 at Week 96 for 301 (n=574, 579)	3.0 (± 13.04)	4.1 (± 13.09)		
Change from BL 301 at Week 120 for 301(n=416, 437)	3.5 (± 13.53)	5.4 (± 12.75)		
Change from BL 301 at Week 144 for 301(n=237, 238)	3.2 (± 13.38)	6.6 (± 13.15)		
Change from BL 301 at Week 144 for 303(n=308, 297)	0.7 (± 14.95)	1.3 (± 13.92)		
Change from BL 301 at Week 168 for 303(n=315, 321)	2.0 (± 14.78)	1.6 (± 14.86)		
Change from BL 301 at Week 192 for 303(n=300, 302)	1.7 (± 15.81)	2.1 (± 15.35)		

Change from BL 301 at Week 216 for 303(n=255, 265)	4.7 (± 15.91)	4.5 (± 14.59)		
Change from BL 301 at Week 240 for 303(n=24, 16)	3.8 (± 11.41)	8.8 (± 9.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 3-Second Paced Auditory Serial Addition Test (PASAT 3) Score in the 205MS303 Treatment Period

End point title	Change from Baseline in 3-Second Paced Auditory Serial Addition Test (PASAT 3) Score in the 205MS303 Treatment Period[20]

End point description:

The PASAT 3 assesses auditory information processing speed. A random series of numbers from 1 to 9, inclusive, are presented and the subject is instructed to consecutively add pairs of numbers so that each number is added to the one that immediately preceded it. In the 3- second PASAT, numbers are presented at a rate of 1 every 3 seconds. The total possible score is the number of correct responses from 0 to 60 (best). A positive change from baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed Study 301 and received at least 1 dose of DAC HYP during Study 303. 'n' is the number of subjects with data available at the given timepoint. No data was collected for subjects from the 203 and 302 studies.

End point type	Secondary

End point timeframe:

Baseline 303, Weeks 12, 24, 48, 120, 144, 168, 192, 216, 240 in Study 303

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: score on a scale				
median (full range (min-max))				
Baseline 303 (n= 595, 604)	54.0 (0 to 60)	54.0 (3 to 60)		
Change to Week 12 (n= 584, 584)	0.0 (-40 to 19)	0.0 (-23 to 25)		
Change to Week 24 (n= 564, 557)	0.0 (-26 to 26)	0.0 (-27 to 39)		
Change to Week 48 (n= 530, 509)	0.0 (-41 to 21)	0.0 (-21 to 41)		
Change to Week 120 (n= 1, 2)	-3.0 (-3 to -3)	-1.0 (-2 to 0)		
Change to Week 144 (n= 305, 301)	-1.0 (-34 to 23)	-1.0 (-31 to 35)		
Change to Week 168 (n= 327, 334)	0.0 (-35 to 21)	0.0 (-30 to 25)		
Change to Week 192 (n= 315, 319)	0.0 (-33 to 26)	0.0 (-42 to 40)		
Change to Week 216 (n= 266, 279)	0.0 (-22 to 16)	0.0 (-23 to 39)		
Change to Week 240 (n= 24, 16)	0.0 (-8 to 12)	-2.0 (-9 to 6)		

Statistical analyses

Statistical analysis title	Analysis 1
Statistical analysis description: Change to Week 12	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3813
Method	ANCOVA

Statistical analysis title	Analysis 2
Statistical analysis description: Change to Week 24	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1679
Method	ANOVA

Statistical analysis title	Analysis 3
Statistical analysis description: Change to Week 48	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5634
Method	ANCOVA

Statistical analysis title	Analysis 4
Statistical analysis description: Change to Week 144	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)

Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7003
Method	ANCOVA

Statistical analysis title	Analysis 5
Statistical analysis description: Change to Week 168	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7812
Method	ANCOVA

Statistical analysis title	Analysis 6
Statistical analysis description: Change to Week 192	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3246
Method	ANCOVA

Statistical analysis title	Analysis 7
Statistical analysis description: Change to Week 216	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6423
Method	ANCOVA

Statistical analysis title	Analysis 8
Statistical analysis description: Change to Week 240	

Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0288
Method	ANCOVA

Secondary: Change from Baseline in 3-Second Paced Auditory Serial Addition Test (PASAT 3) Score in the 205MS301-303 Combined Study Period

End point title	Change from Baseline in 3-Second Paced Auditory Serial Addition Test (PASAT 3) Score in the 205MS301-303 Combined Study Period[21]

End point description:

The PASAT 3 assesses auditory information processing speed. A random series of numbers from 1 to 9, inclusive, are presented and the subject is instructed to consecutively add pairs of numbers so that each number is added to the one that immediately preceded it. In the 3- second PASAT, numbers are presented at a rate of 1 every 3 seconds. The total possible score is the number of correct responses from 0 to 60 (best). A positive change from baseline indicates improvement. 301-303 ITT Population consisted of all subjects who completed study 301 and had at least 1 dose of DAC HYP during study 303. 'n' is the number of subjects with data available at the given timepoint. '999999' indicates that no data was collected.

End point type	Secondary

End point timeframe:

Baseline 301, Weeks 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156 in the 301 study, Baseline 303, Weeks 12, 24, 48, 120, 144,168, 192, 216, 240 in 303 study

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Not all arms in the baseline period are applicable to this endpoint.

End point values	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	597	606		
Units: score on a scale				
median (full range (min-max))				
Baseline 301 (n= 596, 605)	50.0 (0 to 60)	51.0 (9 to 60)		
Change from BL 301 to Week 12 for 301 (n=593, 603)	0.0 (-58 to 40)	1.0 (-59 to 25)		
Change from BL 301 to Week 24 for 301 (n=594, 600)	0.5 (-26 to 31)	1.0 (-32 to 22)		
Change from BL 301 to Week 36 for 301 (n=594, 599)	1.0 (-29 to 30)	1.0 (-37 to 28)		
Change from BL 301 to Week 48 for 301 (n=592, 602)	1.0 (-25 to 42)	1.0 (-38 to 30)		
Change from BL 301 to Week 60 for 301 (n=589, 599)	1.0 (-46 to 40)	2.0 (-34 to 37)		
Change from BL 301 to Week 72 for 301 (n=592, 600)	2.0 (-20 to 40)	2.0 (-21 to 41)		
Change from BL 301 to Week 84 for 301 (n=591, 598)	2.0 (-31 to 39)	2.0 (-41 to 29)		

Change from BL 301 to Week 96 for 301 (n=594, 600)	2.0 (-28 to 41)	2.0 (-25 to 38)		
Change from BL 301 to Week 108 for 301(n=489, 500)	1.0 (-27 to 43)	2.0 (-25 to 40)		
Change from BL 301 to Week 120 for 301(n=397, 397)	2.0 (-27 to 35)	2.0 (-31 to 41)		
Change from BL 301 to Week 132 for 301(n=273, 289)	2.0 (-30 to 35)	2.0 (-19 to 38)		
Change from BL 301 to Week 144 for 301(n=210, 204)	2.0 (-25 to 31)	3.0 (-21 to 31)		
Change from BL 301 to Week 156 for 301(n=0, 1)	999999 (999999 to 999999)	-4.0 (-4 to -4)		
Change from BL 301 to BL 303 (n=595, 603)	2.0 (-34 to 44)	2.0 (-41 to 45)		
Change from BL 301 to Week 12 for 303 (n=582, 580)	2.0 (-38 to 43)	2.0 (-26 to 41)		
Change from BL 301 to Week 24 for 303 (n=562, 553)	2.0 (-31 to 40)	2.0 (-27 to 43)		
Change from BL 301 to Week 48 for 303 (n=528, 505)	2.0 (-47 to 44)	2.0 (-24 to 41)		
Change from BL 301 to Week 120 for 303(n=1, 2)	15.0 (15 to 15)	3.0 (1 to 5)		
Change from BL 301 to Week 144 for 303(n=303, 298)	1.0 (-32 to 37)	2.0 (-24 to 38)		
Change from BL 301 to Week 168 for 303(n=325, 330)	2.0 (-36 to 42)	2.0 (-29 to 42)		
Change from BL 301 to Week 192 for 303(n=313, 316)	2.0 (-40 to 42)	2.0 (-21 to 42)		
Change from BL 301 to Week 216 for 303(n=265, 277)	2.0 (-27 to 40)	2.0 (-30 to 41)		
Change from BL 301 to Week 240 for 303(n=24, 16)	1.5 (-10 to 26)	0.5 (-11 to 23)		

Statistical analyses

Statistical analysis title	Analysis 1
Statistical analysis description:	
Change from Baseline 301 to Week 12 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2567
Method	ANCOVA

Statistical analysis title	Analysis 2
Statistical analysis description:	
Change from Baseline 301 to Week 24 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)

Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6152
Method	ANCOVA

Statistical analysis title	Analysis 3
Statistical analysis description: Change from Baseline 301 to Week 36 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2024
Method	ANCOVA

Statistical analysis title	Analysis 4
Statistical analysis description: Change from Baseline 301 to Week 48 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9988
Method	ANCOVA

Statistical analysis title	Analysis 5
Statistical analysis description: Change from Baseline 301 to Week 60 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7962
Method	ANCOVA

Statistical analysis title	Analysis 6
Statistical analysis description: Change from Baseline 301 to Week 72 for 301	

Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8486
Method	ANCOVA

Statistical analysis title	Analysis 7
Statistical analysis description:	
Change from Baseline 301 to Week 84 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4478
Method	ANCOVA

Statistical analysis title	Analysis 8
Statistical analysis description:	
Change from Baseline 301 to Week 96 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.325
Method	ANCOVA

Statistical analysis title	Analysis 9
Statistical analysis description:	
Change from Baseline 301 to Week 108 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.129
Method	ANCOVA

Statistical analysis title	Analysis 10

Statistical analysis description:	
Change from Baseline 301 to Week 120 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7295
Method	ANCOVA

Statistical analysis title	Analysis 11
Statistical analysis description:	
Change from Baseline 301 to Week 132 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8647
Method	ANCOVA

Statistical analysis title	Analysis 12
Statistical analysis description:	
Change from Baseline 301 to Week 144 for 301	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2183
Method	ANCOVA

Statistical analysis title	Analysis 13
Statistical analysis description:	
Change from Baseline 301 to Baseline 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3945
Method	ANCOVA

Statistical analysis title	Analysis 14
Statistical analysis description: Change from Baseline 301 to Week 12 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5068
Method	ANCOVA

Statistical analysis title	Analysis 15
Statistical analysis description: Change from Baseline 301 to Week 24 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1669
Method	ANCOVA

Statistical analysis title	Analysis 16
Statistical analysis description: Change from Baseline 301 to Week 48 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5038
Method	ANCOVA

Statistical analysis title	Analysis 17
Statistical analysis description: Change from Baseline 301 to Week 144 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6001
Method	ANCOVA

Statistical analysis title	Analysis 18
Statistical analysis description: Change from Baseline 301 to Week 168 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8617
Method	ANCOVA

Statistical analysis title	Analysis 19
Statistical analysis description: Change from Baseline 301 to Week 192 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.259
Method	ANCOVA

Statistical analysis title	Analysis 20
Statistical analysis description: Change from Baseline 301 to Week 216 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)
Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5159
Method	ANCOVA

Statistical analysis title	Analysis 21
Statistical analysis description: Change from Baseline 301 to Week 240 for 303	
Comparison groups	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303) v DAC HYP 150 mg (301) /DAC HYP 150 mg (303)

Number of subjects included in analysis	1203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6123
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First dose of study drug in study 205MS303 to within 180 days of last dose (up to approximately 5.5 years)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)

Reporting group description:

DAC HYP 150 mg SC injection every 4 weeks for up to 4.6 years in this long-term extension study 303; includes subjects who previously received interferon beta-1a (IFN β-1a) 30 µg intramuscular (IM) injection once weekly in study 301 every 4 weeks for up to 144 weeks.

Reporting group title	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)

Reporting group description:

DAC HYP 150 mg subcutaneous (SC) injection every 4 weeks for up to 4.6 years in this long-term extension study 205MS303 (303); includes subjects who previously received DAC HYP 150 mg SC injection in Study 205MS301 (301) every 4 weeks for up to 144 weeks.

Reporting group title	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)

Reporting group description:

DAC HYP 150 mg SC injection every 4 weeks for up to 93.7 weeks in this long-term extension study 303 (subjects started at Week 144 of the study); includes subjects who previously received DAC HYP 150 mg SC injection in study 205MS302 (302) every 4 weeks for up to 24 weeks followed by a 20-week washout period then continued treatment for up to an additional 3 years.

Reporting group title	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)

Reporting group description:

DAC HYP 150 mg SC injection every 4 weeks for up to 94. 1 weeks in this long-term extension study 303 (subjects started at Week 144 of the study); includes subjects who previously received DAC HYP 150 mg SC injection in study 205MS203 (203) every 4 weeks for up to 288 weeks.

Serious adverse events	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)
Total subjects affected by serious adverse events			
subjects affected / exposed	157 / 597 (26.30%)	190 / 606 (31.35%)	15 / 70 (21.43%)
number of deaths (all causes)	2	4	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Anorectal human papilloma virus infection			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
B-cell lymphoma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Breast cancer			
subjects affected / exposed	3 / 597 (0.50%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
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 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Meningioma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Metaplastic breast carcinoma			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Ovarian cancer			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Ovarian fibroma			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parathyroid tumour benign			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Testicular neoplasm			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 597 (0.00%)	4 / 606 (0.66%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyosarcoma			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Vascular disorders			
Granulomatosis with polyangiitis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Kawasaki's disease			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Varicose vein			
subjects affected / exposed	2 / 597 (0.34%)	0 / 606 (0.00%)	0 / 70 (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
Surgical and medical procedures			
Abdominoplasty			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Female sterilisation			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Hospitalisation			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Immunosuppressant drug therapy			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastectomy			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Pregnancy, puerperium and perinatal conditions			

Abortion spontaneous			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Blighted ovum			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Foetal growth restriction			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Premature delivery			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Device dislocation			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Inflammation			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ disorder			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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

Multi-organ failure			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pain			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
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	3 / 597 (0.50%)	3 / 606 (0.50%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 3	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Sarcoidosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Serum sickness			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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			
Adnexal torsion			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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

Cervical dysplasia			
subjects affected / exposed	2 / 597 (0.34%)	0 / 606 (0.00%)	0 / 70 (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
Dysfunctional uterine bleeding			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial hyperplasia			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Endometriosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Metrorrhagia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 adhesion			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Ovarian cyst			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 ruptured			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Pelvic prolapse			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Uterine haemorrhage			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 polyp			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 distress syndrome			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Asthma			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Bronchial hyperreactivity			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	1 / 70 (1.43%)
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 chronic			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Choking			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 obstructive pulmonary disease			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Nasal polyps			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Pharyngeal necrosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Pneumothorax			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Pulmonary sarcoidosis			
subjects affected / exposed	0 / 597 (0.00%)	3 / 606 (0.50%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Tracheal fistula			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Anxiety			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Bipolar i disorder			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Depression			
subjects affected / exposed	2 / 597 (0.34%)	0 / 606 (0.00%)	0 / 70 (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
Personality disorder			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Psychotic disorder			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Somatoform disorder			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Suicide attempt			
subjects affected / exposed	2 / 597 (0.34%)	3 / 606 (0.50%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 597 (0.17%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 597 (0.17%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Diagnostic procedure			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Hepatic enzyme increased			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Liver function test abnormal			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Protein urine present			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Weight decreased			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Ankle fracture			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Concussion			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Contusion			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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 / 597 (0.17%)	7 / 606 (1.16%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (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
Fibula fracture			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Foot fracture			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (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
Hand fracture			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Intentional overdose			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Jaw fracture			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Joint injury			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Ligament injury			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Ligament rupture			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Limb injury			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Lower limb fracture			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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 fractures			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
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	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (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
Snake bite			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Subdural haematoma			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Tibia fracture			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Ulna fracture			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Wrist fracture			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Angina unstable			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiomyopathy			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Left ventricular hypertrophy			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Myocardial infarction			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Nervous system disorders			
Brain compression			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Brain oedema			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Carpal tunnel syndrome			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar syndrome			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral venous thrombosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Convulsion			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Encephalitis autoimmune			

subjects affected / exposed	3 / 597 (0.50%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	2 / 597 (0.34%)	3 / 606 (0.50%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-barre syndrome			
subjects affected / exposed	2 / 597 (0.34%)	0 / 606 (0.00%)	0 / 70 (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
Headache			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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	3 / 597 (0.50%)	3 / 606 (0.50%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple sclerosis relapse			
subjects affected / exposed	61 / 597 (10.22%)	65 / 606 (10.73%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	4 / 113	4 / 117	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle spasticity			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Myasthenia gravis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Neurological symptom			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Optic neuritis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Status epilepticus			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 597 (0.17%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 597 (0.17%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Anaemia			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Granulocytopenia			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Haemolytic anaemia			
subjects affected / exposed	2 / 597 (0.34%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Lymphadenitis			
subjects affected / exposed	2 / 597 (0.34%)	3 / 606 (0.50%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	4 / 597 (0.67%)	10 / 606 (1.65%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	2 / 4	11 / 13	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoid tissue hyperplasia			
subjects affected / exposed	4 / 597 (0.67%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	3 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphopenia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Pancytopenia			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pernicious anaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Pseudolymphoma			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Thrombocytopenia			

subjects affected / exposed	3 / 597 (0.50%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Vertigo			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Eye disorders			
Eye haemorrhage			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Iritis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Retinal detachment			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Abdominal pain upper			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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

Anorectal disorder			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coeliac disease			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (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
Colitis ulcerative			
subjects affected / exposed	2 / 597 (0.34%)	0 / 606 (0.00%)	0 / 70 (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
Constipation			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Crohn's disease			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Diarrhoea			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Diverticulum			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Duodenal ulcer			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Enteritis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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 ulcer			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingivitis ulcerative			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Haemorrhoids			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Inflammatory bowel disease			

subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
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	2 / 597 (0.34%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Large intestine perforation			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Pancreatitis			
subjects affected / exposed	2 / 597 (0.34%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	3 / 597 (0.50%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic ulcer haemorrhage			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Stomatitis necrotising			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Tongue necrosis			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Umbilical hernia			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	2 / 597 (0.34%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Cholelithiasis			
subjects affected / exposed	5 / 597 (0.84%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic hepatitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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	4 / 597 (0.67%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	4 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic necrosis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 toxic			
subjects affected / exposed	1 / 597 (0.17%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Liver injury			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Alopecia scarring			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Dermatitis atopic			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Dermatitis contact			
subjects affected / exposed	3 / 597 (0.50%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Drug reaction with eosinophilia and systemic symptoms			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Eczema			
subjects affected / exposed	2 / 597 (0.34%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema multiforme			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema nodosum			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Henoch-schonlein purpura			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Hidradenitis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Pemphigoid			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Perivascular dermatitis			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Photosensitivity reaction			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Pityriasis rosea			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Psoriasis			
subjects affected / exposed	3 / 597 (0.50%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	3 / 4	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Rash generalised			
subjects affected / exposed	0 / 597 (0.00%)	3 / 606 (0.50%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	2 / 597 (0.34%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rosacea			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Seborrhoeic dermatitis			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Stevens-johnson syndrome			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Toxic epidermal necrolysis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Toxic skin eruption			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Hypertonic bladder			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Nephrolithiasis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Renal colic			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (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
Renal cyst			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Renal failure			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
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 failure acute			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Renal failure chronic			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 retention			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Urogenital fistula			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Vesicoureteric reflux			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Endocrine disorders			
Goitre			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Hyperparathyroidism primary			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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 and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Fibromyalgia			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Foot deformity			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Haemarthrosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Juvenile idiopathic arthritis			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Ligament laxity			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Muscular weakness			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Osteochondrosis			
subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoriatic arthropathy			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Rheumatoid arthritis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Rotator cuff syndrome			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Seronegative arthritis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Spondylolisthesis			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Still's disease adult onset			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Synovitis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Systemic sclerosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Tendonitis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Tenosynovitis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Appendicitis			
subjects affected / exposed	1 / 597 (0.17%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			

subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Bartholin's abscess			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Brucellosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Chlamydial infection			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Chronic hepatitis c			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Cytomegalovirus infection			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Erysipelas			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Genitourinary tract infection			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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 e			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Infection			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (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
Intervertebral discitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Lobar pneumonia			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Lyme disease			

subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Myelitis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Parotitis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Pneumonia			
subjects affected / exposed	5 / 597 (0.84%)	8 / 606 (1.32%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 5	3 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Pulmonary tuberculosis			
subjects affected / exposed	2 / 597 (0.34%)	0 / 606 (0.00%)	0 / 70 (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
Pyelonephritis			
subjects affected / exposed	1 / 597 (0.17%)	1 / 606 (0.17%)	0 / 70 (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
Reiter's syndrome			

subjects affected / exposed	0 / 597 (0.00%)	0 / 606 (0.00%)	0 / 70 (0.00%)
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 tract infection			
subjects affected / exposed	1 / 597 (0.17%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonellosis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Sepsis			
subjects affected / exposed	0 / 597 (0.00%)	2 / 606 (0.33%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	2 / 597 (0.34%)	1 / 606 (0.17%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Tonsillitis			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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 respiratory tract infection			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Urinary tract infection			

subjects affected / exposed	6 / 597 (1.01%)	3 / 606 (0.50%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	4 / 7	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 597 (0.34%)	0 / 606 (0.00%)	0 / 70 (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
Vaginal infection			
subjects affected / exposed	0 / 597 (0.00%)	1 / 606 (0.17%)	0 / 70 (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
Viral infection			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperamylasaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Hypokalaemia			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Type 1 diabetes mellitus			

subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 597 (0.17%)	0 / 606 (0.00%)	0 / 70 (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

Serious adverse events	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)		
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 227 (16.74%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anorectal human papilloma virus infection			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
B-cell lymphoma			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast cancer			

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometrial cancer				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fibroadenoma of breast				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Invasive ductal breast carcinoma				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningioma				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metaplastic breast carcinoma				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cancer				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian fibroma				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parathyroid tumour benign				

subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Testicular neoplasm			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyosarcoma			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Granulomatosis with polyangiitis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Kawasaki's disease			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Varicose vein			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			

Abdominoplasty				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Female sterilisation				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hospitalisation				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immunosuppressant drug therapy				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mastectomy				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Abortion spontaneous				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blighted ovum				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foetal growth restriction				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Premature delivery				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device dislocation				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inflammation				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multi-organ disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multi-organ failure				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sarcoidosis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Serum sickness			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Adnexal torsion			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervical dysplasia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysfunctional uterine bleeding			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endometrial hyperplasia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Endometriosis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metrorrhagia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian adhesion			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst ruptured			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pelvic prolapse			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine haemorrhage			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine polyp			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Acute respiratory distress syndrome				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchial hyperreactivity				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis chronic				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Choking				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasal polyps				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngeal necrosis				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary fibrosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary sarcoidosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheal fistula				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Acute stress disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anxiety				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bipolar i disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Personality disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Somatoform disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				

subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diagnostic procedure			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver function test abnormal			
subjects affected / exposed	1 / 227 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Protein urine present			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Weight decreased			

subjects affected / exposed	1 / 227 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	1 / 227 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clavicle fracture			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	2 / 227 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibula fracture			

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hand fracture				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intentional overdose				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaw fracture				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint injury				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ligament injury				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament rupture				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Limb injury				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meniscus injury				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Snake bite				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic intracranial haemorrhage				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ulna fracture				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina pectoris				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular hypertrophy				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain compression				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain oedema				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Carpal tunnel syndrome				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebellar syndrome				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral venous thrombosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalitis autoimmune				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Guillain-barre syndrome				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				

subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis relapse			
subjects affected / exposed	17 / 227 (7.49%)		
occurrences causally related to treatment / all	0 / 20		
deaths causally related to treatment / all	0 / 0		
Muscle spasticity			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myasthenia gravis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neurological symptom			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Optic neuritis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			

subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Granulocytopenia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemolytic anaemia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenopathy			
subjects affected / exposed	2 / 227 (0.88%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Lymphoid tissue hyperplasia			

subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphopenia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pernicious anaemia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pseudolymphoma			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Acute vestibular syndrome			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertigo			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

Eye haemorrhage				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Iritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal detachment				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anorectal disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coeliac disease				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ulcerative				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Crohn's disease				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulum				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Functional gastrointestinal disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorder				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gingivitis ulcerative				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inflammatory bowel disease				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peptic ulcer haemorrhage				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis necrotising				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tongue necrosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic hepatitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic necrosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis cholestatic				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis toxic				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaundice				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver injury				

subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Alopecia scarring			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dermatitis atopic			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dermatitis contact			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug eruption			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eczema			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erythema			
subjects affected / exposed	1 / 227 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erythema multiforme			

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erythema nodosum				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Henoch-schonlein purpura				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hidradenitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pemphigoid				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perivascular dermatitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Photosensitivity reaction				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pityriasis rosea				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psoriasis				

subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash generalised				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash maculo-papular				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rosacea				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seborrhoeic dermatitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stevens-johnson syndrome				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxic epidermal necrolysis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxic skin eruption				

subjects affected / exposed	1 / 227 (0.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertonic bladder			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal cyst			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 227 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure chronic			

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tubulointerstitial nephritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urogenital fistula				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vesicoureteric reflux				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Goitre				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperparathyroidism primary				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Back pain				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fibromyalgia				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot deformity				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemarthrosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Juvenile idiopathic arthritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ligament laxity				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteochondrosis				

subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psoriatic arthropathy				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rheumatoid arthritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seronegative arthritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spondylolisthesis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Still's disease adult onset				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Synovitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic sclerosis				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendonitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tenosynovitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Anal abscess				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bartholin's abscess				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brucellosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chlamydial infection				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic hepatitis c				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Genitourinary tract infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis e				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral discitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lobar pneumonia				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lyme disease				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis aseptic				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parotitis				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia cytomegaloviral				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reiter's syndrome				
subjects affected / exposed	1 / 227 (0.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Salmonellosis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vaginal infection				
subjects affected / exposed	0 / 227 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				

subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperamylasaemia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 227 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	IFN β-1a 30 µg (301)/DAC HYP 150 mg (303)	DAC HYP 150 mg (301) /DAC HYP 150 mg (303)	DAC HYP 150 mg (302) /DAC HYP 150 mg (303)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	463 / 597 (77.55%)	476 / 606 (78.55%)	42 / 70 (60.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	45 / 597 (7.54%)	48 / 606 (7.92%)	3 / 70 (4.29%)
occurrences (all)	59	65	3
Aspartate aminotransferase increased			
subjects affected / exposed	40 / 597 (6.70%)	48 / 606 (7.92%)	2 / 70 (2.86%)
occurrences (all)	48	72	2
Liver function test abnormal			
subjects affected / exposed	32 / 597 (5.36%)	30 / 606 (4.95%)	2 / 70 (2.86%)
occurrences (all)	32	34	2
Nervous system disorders			
Headache			
subjects affected / exposed	57 / 597 (9.55%)	56 / 606 (9.24%)	7 / 70 (10.00%)
occurrences (all)	93	92	13
Multiple sclerosis relapse			
subjects affected / exposed	179 / 597 (29.98%)	169 / 606 (27.89%)	15 / 70 (21.43%)
occurrences (all)	339	282	28
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	47 / 597 (7.87%)	71 / 606 (11.72%)	3 / 70 (4.29%)
occurrences (all)	65	93	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	40 / 597 (6.70%)	41 / 606 (6.77%)	3 / 70 (4.29%)
occurrences (all)	45	51	3
Pyrexia			
subjects affected / exposed	45 / 597 (7.54%)	43 / 606 (7.10%)	3 / 70 (4.29%)
occurrences (all)	77	58	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	42 / 597 (7.04%)	35 / 606 (5.78%)	2 / 70 (2.86%)
occurrences (all)	51	48	2
Toothache			

subjects affected / exposed	17 / 597 (2.85%)	14 / 606 (2.31%)	4 / 70 (5.71%)
occurrences (all)	18	17	4
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	13 / 597 (2.18%)	16 / 606 (2.64%)	4 / 70 (5.71%)
occurrences (all)	19	16	4
Eczema			
subjects affected / exposed	32 / 597 (5.36%)	46 / 606 (7.59%)	1 / 70 (1.43%)
occurrences (all)	52	71	2
Erythema			
subjects affected / exposed	31 / 597 (5.19%)	27 / 606 (4.46%)	0 / 70 (0.00%)
occurrences (all)	33	35	0
Rash			
subjects affected / exposed	39 / 597 (6.53%)	64 / 606 (10.56%)	0 / 70 (0.00%)
occurrences (all)	52	88	0
Psychiatric disorders			
Depression			
subjects affected / exposed	45 / 597 (7.54%)	38 / 606 (6.27%)	1 / 70 (1.43%)
occurrences (all)	52	43	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	45 / 597 (7.54%)	38 / 606 (6.27%)	3 / 70 (4.29%)
occurrences (all)	49	53	3
Back pain			
subjects affected / exposed	65 / 597 (10.89%)	51 / 606 (8.42%)	3 / 70 (4.29%)
occurrences (all)	78	73	3
Pain in extremity			
subjects affected / exposed	34 / 597 (5.70%)	40 / 606 (6.60%)	2 / 70 (2.86%)
occurrences (all)	42	48	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	29 / 597 (4.86%)	36 / 606 (5.94%)	3 / 70 (4.29%)
occurrences (all)	35	39	3
Influenza			
subjects affected / exposed	46 / 597 (7.71%)	35 / 606 (5.78%)	1 / 70 (1.43%)
occurrences (all)	56	44	1

Nasopharyngitis			
subjects affected / exposed	121 / 597 (20.27%)	125 / 606 (20.63%)	6 / 70 (8.57%)
occurrences (all)	267	283	9
Oral herpes			
subjects affected / exposed	42 / 597 (7.04%)	35 / 606 (5.78%)	3 / 70 (4.29%)
occurrences (all)	84	61	5
Pharyngitis			
subjects affected / exposed	53 / 597 (8.88%)	47 / 606 (7.76%)	1 / 70 (1.43%)
occurrences (all)	68	61	2
Sinusitis			
subjects affected / exposed	41 / 597 (6.87%)	26 / 606 (4.29%)	1 / 70 (1.43%)
occurrences (all)	60	36	1
Tonsillitis			
subjects affected / exposed	34 / 597 (5.70%)	14 / 606 (2.31%)	4 / 70 (5.71%)
occurrences (all)	48	18	4
Upper respiratory tract infection			
subjects affected / exposed	116 / 597 (19.43%)	114 / 606 (18.81%)	13 / 70 (18.57%)
occurrences (all)	226	216	19
Urinary tract infection			
subjects affected / exposed	77 / 597 (12.90%)	58 / 606 (9.57%)	4 / 70 (5.71%)
occurrences (all)	111	109	7

Non-serious adverse events	DAC HYP 150 mg (203) /DAC HYP 150 mg (303)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 227 (51.10%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	16 / 227 (7.05%)		
occurrences (all)	22		
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 227 (4.85%)		
occurrences (all)	15		
Liver function test abnormal			
subjects affected / exposed	6 / 227 (2.64%)		
occurrences (all)	6		
Nervous system disorders			

Headache subjects affected / exposed occurrences (all) Multiple sclerosis relapse subjects affected / exposed occurrences (all)	16 / 227 (7.05%) 31 36 / 227 (15.86%) 51		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	7 / 227 (3.08%) 12		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	4 / 227 (1.76%) 5 7 / 227 (3.08%) 13		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all)	10 / 227 (4.41%) 16 3 / 227 (1.32%) 3		
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Rash	4 / 227 (1.76%) 5 5 / 227 (2.20%) 6 1 / 227 (0.44%) 1		

subjects affected / exposed	9 / 227 (3.96%)		
occurrences (all)	11		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 227 (0.44%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 227 (3.08%)		
occurrences (all)	7		
Back pain			
subjects affected / exposed	10 / 227 (4.41%)		
occurrences (all)	11		
Pain in extremity			
subjects affected / exposed	2 / 227 (0.88%)		
occurrences (all)	3		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 227 (0.44%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	4 / 227 (1.76%)		
occurrences (all)	4		
Nasopharyngitis			
subjects affected / exposed	18 / 227 (7.93%)		
occurrences (all)	25		
Oral herpes			
subjects affected / exposed	6 / 227 (2.64%)		
occurrences (all)	10		
Pharyngitis			
subjects affected / exposed	9 / 227 (3.96%)		
occurrences (all)	13		
Sinusitis			
subjects affected / exposed	4 / 227 (1.76%)		
occurrences (all)	4		
Tonsillitis			

subjects affected / exposed	2 / 227 (0.88%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	26 / 227 (11.45%)		
occurrences (all)	36		
Urinary tract infection			
subjects affected / exposed	10 / 227 (4.41%)		
occurrences (all)	12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 September 2018	Study was terminated early because the subject population under study was no longer the same as indicated for use in the majority of countries.	-

Notes:

Limitations and caveats

None reported