Clinical trial results:
A Multicenter, Open-label, Extension Study to Evaluate the Long Term Safety and Efficacy of Daclizumab High Yield Process (DAC HYP) Monotherapy in Subjects With Multiple Sclerosis Who Have Completed Treatment in Study 205MS202 (SELECTION)

Summary

EudraCT number	2009-015318-23
Trial protocol	CZ GB DE HU
Global end of trial date	25 August 2016

Results information

Result version number	v1 (current)
This version publication date	10 September 2017
First version publication date	10 September 2017

Trial information

Trial identification

Sponsor protocol code	205-MS-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01051349
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, +1 866-633-4636, clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen, +1 866-633-4636, 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	25 August 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 August 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the safety of extended treatment with DAC HYP monotherapy in participants with relapsing-remitting multiple sclerosis (RRMS). The secondary objectives of this study were to assess the long-term immunogenicity of DAC HYP and the durability of response to DAC HYP in preventing multiple sclerosis (MS) relapse, slowing disability progression, and reducing new MS lesion formation in this study population.

Protection of trial subjects:

Written informed consent was obtained from each participant prior to evaluations performed for eligibility. Participants 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 105
Country: Number of subjects enrolled	Poland: 100
Country: Number of subjects enrolled	Czech Republic: 63
Country: Number of subjects enrolled	Ukraine: 57
Country: Number of subjects enrolled	Hungary: 44
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	India: 11
Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	410
EEA total number of subjects	237

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)	410
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 410 enrolled participants, 60 participants who received at least 6 consecutive monthly doses of DAC HYP in this study and had provided written informed consent were enrolled in to the autoinjector substudy and 91 participants who received seasonal trivalent influenza vaccine were enrolled in vaccine substudy (exploratory analyses).

Period 1

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

Arms

Arm title	BIIB019

Arm description:

Participants received BIIB019, 150 mg subcutaneous injection every 4 weeks up to Week 276.

Arm type	Experimental
Investigational medicinal product name	BIIB019
Investigational medicinal product code	
Other name	Daclizumab high-yield process (DAC HYP)
Pharmaceutical forms	Solution for injection/infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

50 mg subcutaneous (SC) injection every 4 weeks.

Number of subjects in period 1	BIIB019
Started	410
Completed	237
Not completed	173
Adverse event, non-fatal	88
Subject non-compliance	7
Investigator Decision	6
Lost to follow-up	6
Reason not Specified	12
Consent Withdrawn	54

Baseline characteristics

Reporting groups	
Reporting group title	BIIB019
Reporting group description:	
Participants received BIIB019, 150 mg subcutaneous injection every 4 weeks up to Week 276.	

Reporting group values	BIIB019	Total	
Number of subjects	410	410	
Age categorical Units: Subjects			
Adults (18-64 years)	410	410	
Age Continuous Units: years			
arithmetic mean	38.4		
standard deviation	± 8.74	-	
Gender, Male/Female Units: Subjects			
Female	254	254	
Male	156	156	

End points

End points reporting groups

Reporting group title	BIIB019
Reporting group description:	
Participants received BIIB019, 150 mg subcutaneous injection every 4 weeks up to Week 276.	
Subject analysis set title	BIIB019 (prefilled syringe [PFS])
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BIIB019, 150 mg subcutaneous injection in a prefilled syringe every 4 weeks up to Week 276.	
Subject analysis set title	BIIB019 (Autoinjector [AI])
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BIIB019, 150 mg subcutaneous injection using an autoinjector every 4 weeks up to Week 276.	

Primary: Percentage of Participants With Adverse Events (AEs), Serious Adverse Events (SAEs), Discontinuation due to AEs, Withdrawals due to AEs

End point title	Percentage of Participants With Adverse Events (AEs), Serious Adverse Events (SAEs), Discontinuation due to AEs, Withdrawals due to AEs[1]
End point description:	
An AE is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. A SAE is any untoward medical occurrence or effect that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, 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.	
End point type	Primary
End point timeframe:	
Baseline up to 24 weeks after last dose of treatment (Up to 300 weeks)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not performed for this endpoint.

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: participants				
Number of participants with an AEs	358			
Number of participants with SAEs	148			
Participants discontinuing treatment due to AE	91			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve Over the Dosing Interval (AUC0-

t) after Dose 4 for Daclizumab

End point title	Area Under the Concentration-Time Curve Over the Dosing Interval (AUC0-t) after Dose 4 for Daclizumab[2]

End point description:

End point type	Primary

End point timeframe:

Day 90 (Week 12) at predose and 8, 24, 72 and 120 hours post-dose and 7, 10, 14, 21 and 28 days post-dose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not performed for this endpoint.

End point values	BIIB019 (prefilled syringe [PFS])	BIIB019 (Autoinjector [AI])		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: hr*mg/mL				
arithmetic mean (standard deviation)	610.5 (± 253.89)	666.8 (± 253.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with New or Newly Enlarging T2 Hyperintense Lesions Compared to Baseline

End point title	Number of Participants with New or Newly Enlarging T2 Hyperintense Lesions Compared to Baseline

End point description:

New or newly enlarging T2 hyperintense lesions evaluated by magnetic resonance imaging (MRI) and analyzed by a central reader.

End point type	Secondary

End point timeframe:

From Baseline through 288 weeks

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: participants				
Week 48 New or newly enlarging T2 lesions=0(n=363)	255			
Week 48 New or newly enlarging T2 lesions=1(n=363)	39			
Week 48 New or newly enlarging T2 lesions=2(n=363)	27			
Week 48 New or newly enlarging T2 lesions=3(n=363)	12			

Week 48 New or newly enlarging T2 lesions=4(n=363)	5			
Week 48 New/newly enlarging T2 lesions=5-6(n=363)	6			
Week 48 New/newly enlarging T2 lesions=7-10(n=363)	8			
Week 48 New/newly enlarging T2 lesions>=11(n=363)	11			
Week 96 New/newly enlarging T2 lesions=0(n=333)	213			
Week 96 New/newly enlarging T2 lesions=1(n=333)	41			
Week 96 New/newly enlarging T2 lesions=2(n=333)	17			
Week 96 New/newly enlarging T2 lesions=3(n=333)	17			
Week 96 New/newly enlarging T2 lesions=4(n=333)	11			
Week 96 New/newly enlarging T2 lesions=5-6(n=333)	6			
Week 96 New/newly enlarging T2 lesions=7-10(n=333)	10			
Week 96 New/newly enlarging T2 lesions>=11(n=333)	18			
Week 144 New/newly enlarging T2 lesions=0(n=53)	33			
Week 144 New/newly enlarging T2 lesions=1(n=53)	5			
Week 144 New/newly enlarging T2 lesions=2(n=53)	1			
Week 144 New/newly enlarging T2 lesions=3(n=53)	2			
Week 144 New/newly enlarging T2 lesions=4(n=53)	1			
Week 144 New/newly enlarging T2 lesions=5-6(n=53)	4			
Week 144 New/newly enlarging T2 lesions=7-10(n=53)	1			
Week 144 New/newly enlarging T2 lesions>=11(n=53)	6			
Week 192 New/newly enlarging T2 lesions=0(n=262)	144			
Week 192 New/newly enlarging T2 lesions=1(n=262)	30			
Week 192 New/newly enlarging T2 lesions=2(n=262)	24			
Week 192 New/newly enlarging T2 lesions=3(n=262)	13			
Week 192 New/newly enlarging T2 lesions=4(n=262)	9			
Week 192 Ne/newly enlarging T2 lesions=5-6(n=262)	11			
Week 192 New/newly enlarging T2lesions=7-10(n=262)	11			
Week 192 New/newly enlarging T2 lesions>=11(n=262)	20			
Week 240 New/newly enlarging T2 lesions=0(n=121)	60			
Week 240 New/newly enlarging T2 lesions=1(n=121)	10			
Week 240 New/newly enlarging T2 lesions=2(n=121)	14			

Week 240 New/newly enlarging T2 lesions=3(n=121)	9			
Week 240 New/newly enlarging T2 lesions=4(n=121)	7			
Week 240 New/newly enlarging T2 lesions=5-6(n=121)	7			
Week 240 New/newly enlarging T2lesions=7-10(n=121)	3			
Week 240 New/newly enlarging T2 lesions>=11(n=121)	11			
Week 288 New/newly enlarging T2 lesions=0(n=27)	14			
Week 288 New/newly enlarging T2 lesions=1(n=27)	1			
Week 288 New/newly enlarging T2 lesions=2(n=27)	4			
Week 288 New/ newly enlarging T2 lesions=3(n=27)	1			
Week 288 New/newly enlarging T2 lesions=4(n=27)	0			
Week 288 New/newly enlarging T2 lesions=5-6(n=27)	1			
Week 288 New/newly enlarging T2 lesions=7-10(n=27)	3			
Week 288 New/newly enlarging T2 lesions>=11(n=27)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Change in Volume of New or Newly Enlarging T2 Hyperintense Lesions Compared to Baseline

End point title	Annual Change in Volume of New or Newly Enlarging T2 Hyperintense Lesions Compared to Baseline
End point description:	
New or newly enlarging T2 hyperintense lesions evaluated by MRI and analyzed by a central reader.	
End point type	Secondary
End point timeframe:	
From Baseline through 288 weeks	

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: mm^3				
arithmetic mean (standard deviation)				
Change from Baseline at Week 48 (n=362)	-340.8 (± 1237.64)			
Change from Baseline at Week 96 (n=330)	-237.7 (± 1382.86)			
Change from Baseline at Week 144 (n=51)	38.2 (± 1825.06)			

Change from Baseline at Week 192 (n=262)	-251.2 (± 2326.41)			
Change from Baseline at Week 240 (n=122)	-269.7 (± 1188.82)			
Change from Baseline at Week 288 (n=27)	31.9 (± 1008.87)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Total Number of New Gadolinium-enhancing Lesions

End point title	Number of Participants with Total Number of New Gadolinium-enhancing Lesions

End point description:

New Gadolinium-enhancing lesions was evaluated by MRI and analyzed by a central reader.

End point type	Secondary

End point timeframe:

From Baseline through 288 weeks

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: participants				
Week 48 new Gd-enhancing lesions=1 (n=372)	22			
Week 48 new Gd-enhancing lesions=2 (n=372)	3			
Week 48 new Gd-enhancing lesions=3 (n=372)	6			
Week 48 new Gd-enhancing lesions=>4 (n=372)	11			
Week 96 new Gd-enhancing lesions=1 (n=338)	14			
Week 96 new Gd-enhancing lesions=2 (n=338)	7			
Week 96 new Gd-enhancing lesions=3 (n=338)	4			
Week 96 new Gd-enhancing lesions=>4 (n=338)	5			
Week 144 new Gd-enhancing lesions=1 (n=55)	1			
Week 144 new Gd-enhancing lesions=2 (n=55)	0			
Week 144 new Gd-enhancing lesions=3 (n=55)	1			
Week 144 new Gd-enhancing lesions=>4 (n=55)	2			
Week 192 new Gd-enhancing lesions=1 (n=266)	13			

Week 192 new Gd-enhancing lesions=2 (n=266)	5			
Week 192 new Gd-enhancing lesions=3 (n=266)	1			
Week 192 new Gd-enhancing lesions=>4 (n=266)	0			
Week 240 new Gd-enhancing lesions=1 (n=124)	5			
Week 240 new Gd-enhancing lesions=2 (n=124)	0			
Week 240 new Gd-enhancing lesions=3 (n=124)	0			
Week 240 new Gd-enhancing lesions=>4 (n=124)	0			
Week 288 new Gd-enhancing lesions=1 (n=27)	2			
Week 288 new Gd-enhancing lesions=2 (n=27)	0			
Week 288 new Gd-enhancing lesions=3 (n=27)	0			
Week 288 new Gd-enhancing lesions=>4 (n=27)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Change in Number of T1 Hypointense Lesions

End point title	Annual Change in Number of T1 Hypointense Lesions

End point description:

T1 hypointense lesions changes reflect tissue destruction. Volume of T1 hypointense lesions is deemed a more valuable assessment. Hence number of T1 hypointense lesions were not assessed and reported.

End point type	Secondary

End point timeframe:

From Baseline through 288 weeks

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Lesions				

Notes:

[3] - This endpoint was not assessed and reported.

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Change in Volume of New Gadolinium-Enhancing Lesions

End point title	Annual Change in Volume of New Gadolinium-Enhancing Lesions

End point description:

Gd enhancing lesion volume reflects acute inflammatory activity. The number of Gd lesions is a more valuable outcome measure. Hence the volume of Gd enhancing lesions was not assessed and reported.

End point type	Secondary

End point timeframe:

From Baseline through 288 weeks

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: mm^3				
arithmetic mean (standard deviation)	()			

Notes:

[4] - This endpoint was not assessed and reported.

Statistical analyses

No statistical analyses for this end point

Secondary: Annual Change in Volume of T1 Hypointense Lesions

End point title	Annual Change in Volume of T1 Hypointense Lesions

End point description:

Volume of T1 hypointense lesions was evaluated by MRI and analyzed by a central reader.

End point type	Secondary

End point timeframe:

From Baseline through 288 weeks

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: mm^3				
arithmetic mean (standard deviation)				
Change from Baseline at Week 48 (n=360)	-183.5 (± 370.66)			
Change from Baseline at Week 96 (n=325)	-160.6 (± 443.78)			
Change from Baseline at Week 144 (n=51)	-142.4 (± 432.57)			
Change from Baseline at Week 192 (n=259)	-115.2 (± 826.84)			
Change from Baseline at Week 240 (n=121)	-140.8 (± 514.38)			
Change from Baseline at Week 288 (n=27)	-148.4 (± 500.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in Total Brain Volume

End point title	Percent Change in Total Brain Volume

End point description:

To assess brain atrophy, total brain volume was be measured by MRI and analyzed by a central reader.

End point type	Secondary

End point timeframe:

From Baseline through 288 weeks

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: mL				
arithmetic mean (standard deviation)				
Change from Week 0 to Week 48 (n=347)	-0.4 (± 1)			
Change from Week 48 to Week 96 (n=303)	-0.4 (± 0.78)			
Change from Week 96 to Week 144 (n=37)	-0.2 (± 1)			
Change from Week 144 to Week 192 (n=30)	-0.5 (± 0.59)			
Change from Week 192 to Week 240 (n=86)	-0.2 (± 0.83)			
Change from Week 240 to Week 288 (n=27)	0.1 (± 0.73)			

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Relapse Rate (ARR)

End point title	Annualized Relapse Rate (ARR)

End point description:

Relapses are defined as new or recurrent neurologic symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurological findings upon examination by the Examining Neurologist. The 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. Adjusted ARR was reported.

End point type	Secondary

End point timeframe:

Week 288

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: relapses per person-year				
number (confidence interval 95%)	0.124 (0.099 to 0.156)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Antibodies to DAC HYP

End point title	Number of Participants with Antibodies to DAC HYP

End point description:

End point type	Secondary

End point timeframe:

Up to Week 288

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	407			
Units: participants	43			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Sustained Disability Progression for 12 Weeks

End point title	Number of Participants with Sustained Disability Progression for 12 Weeks

End point description:

Sustained disability progression defined by at least a 1.0-point increase on the Expanded Disability Status Scale (EDSS) from a baseline EDSS ≥1.0 that is sustained for 12 weeks, or at least a 1.5-point increase on the EDSS from a baseline EDSS <1.0 that is sustained for 12 weeks. The EDSS measures the disability status of people with multiple sclerosis on a scale that ranges from 0 to 10, with higher scores indicating more disability.

End point type	Secondary

End point timeframe:

Week 48 up to Week 288

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: participants				
Weeks 0 - 48	22			
Weeks 49 - 96	17			
Weeks 97 - 144	13			
Weeks 145 -192	7			
Week 193 - 288	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Sustained Disability Progression for 24 Weeks

End point title	Number of Participants with Sustained Disability Progression for 24 Weeks

End point description:

Sustained disability progression defined by at least a 1.0-point increase on the Expanded Disability Status Scale (EDSS) from a baseline EDSS ≥1.0 that is sustained for 24 weeks, or at least a 1.5-point increase on the EDSS from a baseline EDSS <1.0 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, with higher scores indicating more disability.

End point type	Secondary

End point timeframe:

Week 48 up to Week 288

End point values	BIIB019			
Subject group type	Reporting group			
Number of subjects analysed	410			
Units: participants				
Weeks 0 - 48	19			
Weeks 49 - 96	18			
Weeks 97 - 144	11			
Weeks 145 -192	7			
Week 193 - 288	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Maximum Concentration (Cmax) after Dose 4 for Daclizumab

End point title	Observed Maximum Concentration (Cmax) after Dose 4 for Daclizumab

End point description:

End point type	Secondary

End point timeframe:

Day 90 (Week 12) at predose and 8, 24, 72 and 120 hours post-dose and 7, 10, 14, 21 and 28 days post-dose

End point values	BIIB019 (prefilled syringe [PFS])	BIIB019 (Autoinjector [AI])		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: mg/mL				
arithmetic mean (standard deviation)	31.8 (± 13.11)	33.6 (± 14.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Concentration (Tmax) for Daclizumab after Dose 4

End point title	Time to Reach Maximum Concentration (Tmax) for Daclizumab after Dose 4

End point description:

End point type	Secondary

End point timeframe:

Day 90 (Week 12) at predose and 8, 24, 72 and 120 hours post-dose and 7, 10, 14, 21 and 28 days post-dose

End point values	BIIB019 (prefilled syringe [PFS])	BIIB019 (Autoinjector [AI])		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: hour				
median (full range (min-max))	5 (1 to 14)	6 (1 to 14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Minimum Concentration (Cmin) for Daclizumab after Dose 4

End point title	Observed Minimum Concentration (Cmin) for Daclizumab after Dose 4

End point description:

End point type	Secondary

End point timeframe:

Day 90 (Week 12) at predose and 8, 24, 72 and 120 hours post-dose and 7, 10, 14, 21 and 28 days post-dose

End point values	BIIB019 (prefilled syringe [PFS])	BIIB019 (Autoinjector [AI])		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: mg/mL				
arithmetic mean (standard deviation)	13.8 (± 7.13)	15.7 (± 7.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Participant-Reported Pain Visual Analog Scale (VAS) Score

End point title	Participant-Reported Pain Visual Analog Scale (VAS) Score

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 participant rates their perceived pain of each injection by placing a vertical mark on the line to indicate the level of pain.

End point type	Secondary

End point timeframe:

First injection (Day 1) and fourth injection (Day 90) 0 hour, 30 minutes, 60 minutes and 8 hours post-dose

End point values	BIIB019 (prefilled syringe [PFS])	BIIB019 (Autoinjector [AI])		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: score on a scale				
arithmetic mean (standard deviation)				
First injection, 0 hour post-dose (n=30, 30)	12.7 (± 17.45)	14.5 (± 19.47)		
First injection, 30 minutes post-dose (n=30,30)	0.1 (± 0.31)	0.4 (± 1.01)		
First injection, 60 minutes post-dose (n=30, 30)	0.1 (± 0.25)	0.3 (± 0.6)		
First injection, 8 hours post-dose (n=30, 30)	0.1 (± 0.25)	0.2 (± 0.5)		
Fourth injection, 0 hour post-dose (n=30, 28)	14.5 (± 21.7)	15.6 (± 24.7)		
Fourth injection, 30 minutes post-dose (n=30, 28)	0.9 (± 3.51)	1.3 (± 3.42)		
Fourth injection, 60 minutes post-dose (n=30, 28)	0 (± 0.18)	0.1 (± 0.31)		
Fourth injection, 8 hours post-dose (n=30, 28)	0.1 (± 0.4)	0.1 (± 0.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Injection Site Assessment Performed by Clinician

End point title	Summary of Injection Site Assessment Performed by Clinician

End point description:

Injection site assessment was performed by clinician and are defined as erythema (redness) rated on a 4 point scale ranging from 0-3, where 0=none, 1=mild, 2=moderate and 3=severe; pigmentation changes (skin discoloration other than redness) rated on a 3 point scale from 0-2, where 0=none, 1=hypopigmentation and 2=hyperpigmentation; induration (swelling) rated on a 4 point scale ranging from 0-3, where 0=none, 1=mild, 2=moderate and 3=severe; tenderness to pressure rated on a 4 point scale ranging from 0-3, where 0=none, 1=mild, 2=moderate and 3=severe; and local temperature changes of injection sites rated on a 3 point scale where 0=normal, 1=warm and 1=hot. Only those score categories for which there was at least 1 participant are reported. Here, Injection=Inj, post-dose=PD

End point type	Secondary

End point timeframe:

First injection (Day 1) and fourth injection (Day 90) 30 minutes; 8, 24, 72, and 120 hours; and 7, 10, and 14 days post-dose

End point values	BIIB019 (prefilled syringe [PFS])	BIIB019 (Autoinjector [AI])		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	30		
Units: participants				
Erythema: Ist Inj 30 min PD: None (n=30,30)	29	29		

Erythema:Ist Inj 30 min PD: Mild (n=30, 30)	1	1		
Erythema: Ist Inj 8 h PD: None (n=30, 30)	30	29		
Erythema:Ist Inj 8 h PD: MIld (n=30, 30)	0	1		
Erythema: Ist Inj 24 h PD: None (n=28,27)	28	27		
Erythema: Ist Inj 72 h PD: None (n=26,26)	26	26		
Erythema: Ist Inj 120 h PD: None (n=26,26)	26	26		
Erythema: Ist Inj 7 days PD: None (n=26,26)	26	26		
Erythema: Ist Inj 10 days PD: None (n=26,26)	26	26		
Erythema: Ist Inj 14 days PD: None (n=26,26)	26	26		
Erythema: 4th Inj 30 min PD: None (n=30,28)	30	27		
Erythema: 4th Inj 30 min PD: Mild (n=30,28)	0	1		
Erythema: 4th Inj 8 h PD: None (n=30,28)	30	28		
Erythema: 4th Inj 24 h PD: None (n=30,27)	30	27		
Erythema: 4th Inj 72 h PD: None (n=29,26)	29	26		
Erythema: 4th Inj 120 h PD: None (n=30,27)	30	27		
Erythema: 4th Inj 7 days PD: None (n=30,28)	30	28		
Erythema: 4th Inj 10 days PD: None (n=30,28)	30	28		
Erythema: 4th Inj 14 days PD: None (n=30,28)	30	28		
Pigmentation: 1st Inj, 30 min PD: None (n=30,30)	30	30		
Pigmentation: 1st Inj, 8 h PD: None (n=30,30)	30	30		
Pigmentation: 1st Inj, 24 h PD: None (n=28, 27)	28	27		
Pigmentation: 1st Inj, 72 h PD: None (n=26, 26)	26	26		
Pigmentation: 1st Inj, 120 h PD: None (n=26, 26)	26	26		
Pigmentation: 1st Inj, 7 days PD: None (n=26, 26)	26	26		
Pigmentation: 1st Inj, 10 days PD: None (n=26, 26)	26	26		
Pigmentation: 1st Inj, 14 days PD: None (n=26, 26)	26	26		
Pigmentation: 4th Inj, 30 min PD: None (n=30,28)	30	28		
Pigmentation: 4th Inj, 8 h PD: None (n=30,28)	30	28		
Pigmentation: 4th Inj, 24 h PD: None (n=30,27)	30	27		
Pigmentation: 4th Inj, 72 h PD: None (n=29,26)	28	26		
Pigmentation: 4th Inj, 72 h PD: Hyper- (n=29,26)	1	0		

Pigmentation: 4th Inj, 120 h PD: None (n=30, 27)	29	27		
Pigmentation: 4th Inj, 120 h PD: Hyper- (n=30, 27)	1	0		
Pigmentation: 4th Inj, 7 days PD: None (n=30, 28)	30	28		
Pigmentation: 4th Inj, 10 days PD: None (n=30, 28)	30	28		
Pigmentation: 4th Inj, 14 days PD: None (n=30, 28)	30	28		
Induration: 1st Inj, 30 min PD: None (n=30, 30)	30	30		
Induration: 1st Inj, 8 h PD: None (n=30, 30)	30	30		
Induration: 1st Inj, 24 h PD: None (n=28, 27)	28	27		
Induration: 1st Inj, 72 h PD: None (n=26, 26)	26	26		
Induration: 1st Inj, 120 h PD: None (n=26, 26)	26	26		
Induration: 1st Inj, 7 days PD: None (n=26, 26)	26	26		
Induration: 1st Inj, 10 days PD: None (n=26, 26)	26	26		
Induration: 1st Inj, 14 days PD: None (n=26, 26)	26	26		
Induration: 4th Inj, 30 min PD: None (n=30, 28)	30	28		
Induration: 4th Inj, 8 h PD: None (n=30, 28)	30	28		
Induration: 4th Inj, 24 h PD: None (n=30, 27)	30	27		
Induration: 4th Inj, 72 h PD: None (n=29, 26)	29	26		
Induration: 4th Inj, 120 h PD: None (n=30, 27)	30	27		
Induration: 4th Inj, 7 days PD: None (n=30, 28)	30	28		
Induration: 4th Inj, 10 days PD: None (n=30, 28)	30	28		
Induration: 4th Inj, 14 days PD: None (n=30, 28)	30	28		
Tenderness: 1st Inj, 30 min PD: None (n=30, 30)	30	29		
Tenderness: 1st Inj, 30 min PD: Mild (n=30, 30)	0	1		
Tenderness: 1st Inj, 8 h PD: None (n=30, 30)	30	30		
Tenderness: 1st Inj, 24 h PD: None (n=28, 27)	28	27		
Tenderness: 1st Inj, 72 h PD: None (n=26, 26)	26	26		
Tenderness: 1st Inj, 120 h PD: None (n=26, 26)	26	26		
Tenderness: 1st Inj, 7 days PD: None (n=26, 26)	26	26		
Tenderness: 1st Inj, 10 days PD: None (n=26, 26)	26	26		
Tenderness: 1st Inj, 14 days PD: None (n=26, 26)	26	26		
Tenderness: 4th Inj, 30 min PD: None (n=30, 28)	30	27		

Tenderness: 4th Inj, 30 min PD: Mild (n=30, 28)	0	1		
Tenderness: 4th Inj, 8 h PD: None (n=30, 28)	30	27		
Tenderness: 4th Inj, 8 h PD: Mild (n=30, 28)	0	1		
Tenderness: 4th Inj, 24 h PD: None (n=30, 27)	30	27		
Tenderness: 4th Inj, 72 h PD: None (n=29, 26)	29	26		
Tenderness: 4th Inj, 120 h PD: None (n=30, 27)	30	27		
Tenderness: 4th Inj, 7 days PD: None (n=30, 28)	30	28		
Tenderness: 4th Inj, 10 days PD: None (n=30, 28)	30	28		
Tenderness: 4th Inj, 14 days PD: None (n=30, 28)	30	28		
Temperature: 1st Inj, 30 min PD: Normal (n=30, 30)	30	30		
Temperature: 1st Inj, 8 h PD: Normal (n=30, 30)	30	30		
Temperature: 1st Inj, 24 h PD: Normal (n=28, 27)	28	27		
Temperature: 1st Inj, 72 h PD: Normal (n=26, 26)	26	26		
Temperature: 1st Inj, 120 h PD: Normal (n=26, 26)	26	26		
Temperature: 1st Inj, 7 days PD: Normal (n=26, 26)	26	26		
Temperature: 1st Inj,10 days PD: Normal (n=26, 26)	26	26		
Temperature: 1st Inj,14 days PD: Normal (n=26, 26)	26	26		
Temperature: 4th Inj, 30 min PD: Normal (n=30, 28)	30	28		
Temperature: 4th Inj, 8 h PD: Normal (n=30, 28)	30	28		
Temperature: 4th Inj, 24 h PD: Normal (n=30, 27)	30	27		
Temperature: 4th Inj, 72 h PD: Normal (n=29, 26)	29	26		
Temperature: 4th Inj, 120 h PD: Normal (n=30, 27)	30	27		
Temperature: 4th Inj, 7 days PD: Normal (n=30, 28)	30	28		
Temperature: 4th Inj,10 days PD: Normal (n=30, 28)	30	28		
Temperature: 4th Inj,14 days PD: Normal (n=30, 28)	30	28		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to 24 weeks after last dose of treatment (Up to 300 weeks)	
Adverse event reporting additional description:	
Treatment emergent AEs are presented regardless of seriousness or relationship to investigational product	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	BIIB019
Reporting group description:	
Participants received BIIB019, 150 mg subcutaneous injection every 4 weeks up to Week 276.	

Serious adverse events	BIIB019		
Total subjects affected by serious adverse events			
subjects affected / exposed	148 / 410 (36.10%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anal cancer			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Benign neoplasm of bladder			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	3 / 410 (0.73%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Clear cell renal cell carcinoma			

subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Carcinoid tumour pulmonary				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intraductal papilloma of breast				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prolactinoma				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
T-cell lymphoma				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Drug detoxification				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eyelid operation				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Mammoplasty				

subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Drug hypersensitivity			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			

subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine inflammation				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Epistaxis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Idiopathic pulmonary fibrosis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Depression				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Aspartate aminotransferase increased				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Cervical vertebral fracture				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				

subjects affected / exposed	2 / 410 (0.49%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pubis fracture			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	2 / 410 (0.49%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Spinal column injury			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	2 / 410 (0.49%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Wound			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis relapse			
subjects affected / exposed	62 / 410 (15.12%)		
occurrences causally related to treatment / all	1 / 112		
deaths causally related to treatment / all	0 / 0		
Neurological decompensation			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular encephalopathy			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Haemolytic anaemia				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic anaemia				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Histiocytosis haematophagic				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Iron deficiency anaemia				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphadenitis				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy				
subjects affected / exposed	6 / 410 (1.46%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Lymphoid tissue hyperplasia				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenic purpura				

subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Choroiditis			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Colitis ulcerative			
subjects affected / exposed	3 / 410 (0.73%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Crohn's disease			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Enterocolitis haemorrhagic			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	2 / 410 (0.49%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus paralytic			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lip oedema			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Obstruction gastric			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	2 / 410 (0.49%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Cholecystitis acute			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholelithiasis			

subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Jaundice hepatocellular				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Liver disorder				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Angioedema				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dermatitis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dermatitis allergic				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Eczema				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug eruption				

subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Erythema nodosum				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Erythrodermic psoriasis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psoriasis				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Photodermatosis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seborrhoeic dermatitis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stevens-johnson syndrome				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Toxic skin eruption				
subjects affected / exposed	3 / 410 (0.73%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Urticaria				

subjects affected / exposed	3 / 410 (0.73%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nephroptosis			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal colic			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis reactive			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Back pain				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc disorder				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Acute sinusitis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				

subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Furuncle				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis c				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	2 / 410 (0.49%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
HIV infection				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infectious mononucleosis				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonsillar abscess				
subjects affected / exposed	1 / 410 (0.24%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	2 / 410 (0.49%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 410 (0.24%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	5 / 410 (1.22%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	2 / 410 (0.49%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	BIIB019		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	296 / 410 (72.20%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	61 / 410 (14.88%)		
occurrences (all)	72		
Aspartate aminotransferase increased			

subjects affected / exposed	49 / 410 (11.95%)		
occurrences (all)	54		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	21 / 410 (5.12%)		
occurrences (all)	27		
Nervous system disorders			
Headache			
subjects affected / exposed	44 / 410 (10.73%)		
occurrences (all)	340		
Multiple sclerosis relapse			
subjects affected / exposed	110 / 410 (26.83%)		
occurrences (all)	189		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	23 / 410 (5.61%)		
occurrences (all)	26		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	25 / 410 (6.10%)		
occurrences (all)	47		
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	32 / 410 (7.80%)		
occurrences (all)	38		
Rash			
subjects affected / exposed	31 / 410 (7.56%)		
occurrences (all)	43		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 410 (5.12%)		
occurrences (all)	40		
Back pain			
subjects affected / exposed	39 / 410 (9.51%)		
occurrences (all)	160		
Infections and infestations			

Bronchitis			
subjects affected / exposed	28 / 410 (6.83%)		
occurrences (all)	37		
Nasopharyngitis			
subjects affected / exposed	68 / 410 (16.59%)		
occurrences (all)	147		
Pharyngitis			
subjects affected / exposed	42 / 410 (10.24%)		
occurrences (all)	66		
Respiratory tract infection viral			
subjects affected / exposed	35 / 410 (8.54%)		
occurrences (all)	55		
Upper respiratory tract infection			
subjects affected / exposed	60 / 410 (14.63%)		
occurrences (all)	142		
Urinary tract infection			
subjects affected / exposed	42 / 410 (10.24%)		
occurrences (all)	90		
Viral infection			
subjects affected / exposed	23 / 410 (5.61%)		
occurrences (all)	30		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2011	• The primary reason for this amendment was to increase subject monitoring for laboratory signals related to hepatic function (Liver function test (LFT) monitoring was increased from every 6 months to monthly throughout the treatment period) and to add criteria for temporary suspension and discontinuation of study treatment for subjects who developed elevations in alanine aminotransferase (ALT), aspartate aminotransferase (AST), or total bilirubin. Subjects who permanently discontinued study treatment due to elevated LFTs were to be evaluated for possible toxicological, infectious, immunological, and metabolic causes of liver injury. • Additional guidance was provided to Investigators on the evaluation and management of cutaneous events. • The use of the DAC HYP PFS was allowed.
05 April 2012	• The primary reason for this amendment was to prohibit concomitant treatment with medications that have an established association with hepatotoxicity or cutaneous hypersensitivity reactions. • Monthly LFT results were provided to the Neurologist prior to administration of study treatment to assess whether treatment suspension criteria were met. • Subjects were provided an additional 3 years of open-label treatment with DAC HYP.
12 December 2012	• The primary reason for this amendment was the addition of the 2013-2014 influenza vaccine substudy
24 May 2013	• The primary reason for this amendment was to reintroduce physical examination, vital signs, hematology, and blood chemistry assessments at Week 96.
13 June 2013	• The primary reason for this amendment was to reintroduce urinalysis assessment at Week 96.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported