



Clinical trial results:

A Dose-Blinded, 2-Dose Level, Parallel-Group, Multicenter, Long-Term Extension Study to Evaluate the Long-Term Safety, Efficacy, and Immunogenicity of BIIB023 in Subjects with Lupus Nephritis

Summary

EudraCT number	2013-000594-69
Trial protocol	BE ES IT HU PL DE
Global end of trial date	15 January 2016

Results information

Result version number	v1 (current)
This version publication date	08 December 2016
First version publication date	08 December 2016

Trial information

Trial identification

Sponsor protocol code	211LE202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01930890
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	15 January 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 January 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the long-term safety and tolerability of BIIB023 in subjects with lupus nephritis (LN).

This was an extension study for all subjects who completed study 211LE201 (2011-002159-32) through Week 52 and did not discontinue BIIB023 or placebo. Eligible subjects from Study 211LE201 were followed for up to 108 weeks.

Subjects who received BIIB023 low dose or high dose in 211LE201 continued to receive the same dosing in this study (211LE202; 2013-000594-69) in addition to background therapy. Subjects who received placebo in 211LE201 were randomized to receive either BIIB023 low dose or high dose in addition to background therapy.

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:

Open-label mycophenolate mofetil (MMF) and oral corticosteroids were used at the Investigator's discretion. MMF could be increased to a maximum of 3 g/day or reduced/discontinued in response to peripheral neutrophil counts and/or serious infection. Corticosteroid therapy was specified as prednisone doses, but equivalent doses of other corticosteroids were permitted. The subjects were to obtain corticosteroid therapy by prescription.

Evidence for comparator: -

Actual start date of recruitment	22 November 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 21
Country: Number of subjects enrolled	Philippines: 14
Country: Number of subjects enrolled	Malaysia: 8
Country: Number of subjects enrolled	Colombia: 7
Country: Number of subjects enrolled	Peru: 7
Country: Number of subjects enrolled	United States: 7
Country: Number of subjects enrolled	Australia: 3

Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Spain: 1
Worldwide total number of subjects	87
EEA total number of subjects	10

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)	87
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who completed Week 52 of Study 211LE201 and did not discontinue BIIB023 or placebo study treatment were eligible for this study.

Pre-assignment

Screening details:

A total of 87 subjects were randomized.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Blinding implementation details:

BIIB023 was prepared and dispensed by an unblinded Pharmacist or an unblinded medically qualified designee (other than the Investigator or co-Investigator). All subjects enrolled in Study 211LE202 were blinded to their dose level.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (211LE201) to BIIB023 3 mg/kg (211LE202)

Arm description:

Subjects who received placebo every 4 weeks (Q4W) plus MMF and oral corticosteroids in 211LE201 and received BIIB023 3 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Arm type	Experimental
Investigational medicinal product name	BIIB023
Investigational medicinal product code	BIIB023
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

BIIB023 was administered by IV infusion over 1 hour, followed by a minimum of 1-hour observation period.

Investigational medicinal product name	mycophenolate mofetil
Investigational medicinal product code	
Other name	MMF, Cellcept
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

MMF was taken orally morning and evening, before meals, and with a glass of water. Subjects who experienced tolerability issues (e.g., nausea or diarrhea) were allowed to receive MMF 3 times daily. MMF could be increased to a maximum of 3 g/day or reduced/discontinued in response to peripheral neutrophil counts and/or serious infection.

Investigational medicinal product name	oral corticosteroid (prednisone or equivalent)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Use of oral corticosteroids was at the Investigator's discretion.

Arm title	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)
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Arm description:

Participants who received BIIB023 3 mg/kg Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 3 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Arm type	Experimental
Investigational medicinal product name	BIIB023
Investigational medicinal product code	BIIB023
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

BIIB023 was administered by IV infusion over 1 hour, followed by a minimum of 1-hour observation period.

Investigational medicinal product name	mycophenolate mofetil
Investigational medicinal product code	
Other name	MMF, Cellcept
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

MMF was taken orally morning and evening, before meals, and with a glass of water. Subjects who experienced tolerability issues (e.g., nausea or diarrhea) were allowed to receive MMF 3 times daily. MMF could be increased to a maximum of 3 g/day or reduced/discontinued in response to peripheral neutrophil counts and/or serious infection.

Investigational medicinal product name	oral corticosteroid (prednisone or equivalent)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Use of oral corticosteroids was at the Investigator's discretion.

Arm title	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)
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Arm description:

Participants who received placebo every 4 weeks (Q4W) plus MMF and oral corticosteroids in 211LE201 and received BIIB023 20 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Arm type	Experimental
Investigational medicinal product name	BIIB023
Investigational medicinal product code	BIIB023
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

BIIB023 was administered by IV infusion over 1 hour, followed by a minimum of 1-hour observation period.

Investigational medicinal product name	mycophenolate mofetil
Investigational medicinal product code	
Other name	MMF, Cellcept
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

MMF was taken orally morning and evening, before meals, and with a glass of water. Subjects who experienced tolerability issues (e.g., nausea or diarrhea) were allowed to receive MMF 3 times daily. MMF could be increased to a maximum of 3 g/day or reduced/discontinued in response to peripheral neutrophil counts and/or serious infection.

Investigational medicinal product name	oral corticosteroid (prednisone or equivalent)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Use of oral corticosteroids was at the Investigator's discretion.

Arm title	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)
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Arm description:

Participants who received BIIB023 20 mg/kg Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 20 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Arm type	Experimental
Investigational medicinal product name	BIIB023
Investigational medicinal product code	BIIB023
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

BIIB023 was administered by IV infusion over 1 hour, followed by a minimum of 1-hour observation period.

Investigational medicinal product name	mycophenolate mofetil
Investigational medicinal product code	
Other name	MMF, Cellcept
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

MMF was taken orally morning and evening, before meals, and with a glass of water. Subjects who experienced tolerability issues (e.g., nausea or diarrhea) were allowed to receive MMF 3 times daily. MMF could be increased to a maximum of 3 g/day or reduced/discontinued in response to peripheral neutrophil counts and/or serious infection.

Investigational medicinal product name	oral corticosteroid (prednisone or equivalent)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Use of oral corticosteroids was at the Investigator's discretion.

Number of subjects in period 1	Placebo (211LE201) to BIIB023 3 mg/kg (211LE202)	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)
Started	14	33	13
Completed	0	0	0
Not completed	14	33	13
Adverse event, serious fatal	-	-	-
Study Termination	14	28	13
Adverse event, non-fatal	-	1	-
Investigator Decision	-	1	-

Consent Withdrawn	-	3	-
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Number of subjects in period 1	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)
Started	27
Completed	0
Not completed	27
Adverse event, serious fatal	1
Study Termination	25
Adverse event, non-fatal	-
Investigator Decision	-
Consent Withdrawn	1

Baseline characteristics

Reporting groups

Reporting group title	Placebo (211LE201) to BIIB023 3 mg/kg (211LE202)
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Reporting group description:

Subjects who received placebo every 4 weeks (Q4W) plus MMF and oral corticosteroids in 211LE201 and received BIIB023 3 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Reporting group title	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)
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Reporting group description:

Participants who received BIIB023 3 mg/kg Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 3 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Reporting group title	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)
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Reporting group description:

Participants who received placebo every 4 weeks (Q4W) plus MMF and oral corticosteroids in 211LE201 and received BIIB023 20 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Reporting group title	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)
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Reporting group description:

Participants who received BIIB023 20 mg/kg Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 20 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Reporting group values	Placebo (211LE201) to BIIB023 3 mg/kg (211LE202)	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)
Number of subjects	14	33	13
Age, Customized Units: participants			
18 to 19 years	0	0	1
20 to 29 years	6	15	6
30 to 39 years	6	11	3
40 to 49 years	2	6	2
50 to 55 years	0	0	1
> 55 years	0	1	0
Gender, Male/Female Units:			
Female	11	29	10
Male	3	4	3

Reporting group values	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)	Total	
Number of subjects	27	87	
Age, Customized Units: participants			
18 to 19 years	1	2	
20 to 29 years	9	36	
30 to 39 years	14	34	
40 to 49 years	1	11	
50 to 55 years	2	3	
> 55 years	0	1	

Gender, Male/Female			
Units:			
Female	25	75	
Male	2	12	

End points

End points reporting groups

Reporting group title	Placebo (211LE201) to BIIB023 3 mg/kg (211LE202)
Reporting group description: Subjects who received placebo every 4 weeks (Q4W) plus MMF and oral corticosteroids in 211LE201 and received BIIB023 3 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.	
Reporting group title	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)
Reporting group description: Participants who received BIIB023 3 mg/kg Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 3 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.	
Reporting group title	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)
Reporting group description: Participants who received placebo every 4 weeks (Q4W) plus MMF and oral corticosteroids in 211LE201 and received BIIB023 20 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.	
Reporting group title	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)
Reporting group description: Participants who received BIIB023 20 mg/kg Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 20 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.	

Primary: Number of Participants Experiencing Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants Experiencing Adverse Events (AEs) and Serious Adverse Events (SAEs) ^[1]
End point description: AEs with a start date on or after the first dose date in study 211LE202. AE: any untoward medical occurrence that does not necessarily have a causal relationship with this treatment. SAE: any untoward medical occurrence that at any dose: results in death; in the view of the Investigator, places the subject at immediate risk of death (a life-threatening event); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/ incapacity; or results in a congenital anomaly/birth defect. An SAE may also be any other medically important event that, in the opinion of the Investigator, may jeopardize the subject or may require intervention to prevent one of the other outcomes listed above.	
End point type	Primary
End point timeframe: Up to Week 108	

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: Descriptive statistics are presented, per protocol.

End point values	Placebo (211LE201) to BIIB023 3 mg/kg (211LE202)	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	33	13	27
Units: participants				
number (not applicable)				
Any event	4	23	7	19

Moderate or severe event	2	12	3	6
Severe event	0	4	1	3
Event related to dose-blinded treatment	1	5	1	4
Event related to MMF	2	8	2	9
Serious event	1	7	4	3
Serious event related to dose-blinded treatment	0	2	1	1
Serious event related to MMF	0	3	1	2
Fatal event	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects Who Discontinued Study Treatment or Withdrew From Study Due to an AE

End point title	Number of Subjects Who Discontinued Study Treatment or Withdrew From Study Due to an AE ^[2]
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End point description:

AEs with a start date on or after the first dose date in study 211LE202. AE: any untoward medical occurrence that does not necessarily have a causal relationship with this treatment. SAE: any untoward medical occurrence that at any dose: results in death; in the view of the Investigator, places the subject at immediate risk of death (a life-threatening event); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/ incapacity; or results in a congenital anomaly/birth defect. An SAE may also be any other medically important event that, in the opinion of the Investigator, may jeopardize the subject or may require intervention to prevent one of the other outcomes listed above.

End point type	Primary
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End point timeframe:

Up to week 108

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: Descriptive statistics are presented, per protocol.

End point values	Placebo (211LE201) to BIIB023 3 mg/kg (211LE202)	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	33	13	27
Units: subjects				
Discontinued treatment due to an AE	0	0	0	0
Withdrew from study due to an AE	0	2	0	1

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 108

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Placebo (211LE201) to BIIB023 3 mg/ kg (211LE202)
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Reporting group description:

Subjects who received placebo Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 3 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Reporting group title	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)
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Reporting group description:

Subjects who received BIIB023 3 mg/kg Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 3 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Reporting group title	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)
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Reporting group description:

Subjects who received placebo Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 20 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Reporting group title	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)
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Reporting group description:

Subjects who received BIIB023 20 mg/kg Q4W plus MMF and oral corticosteroids in 211LE201 and received BIIB023 20 mg/kg IV Q4W plus MMF and oral corticosteroids through Week 100 in 211LE202.

Serious adverse events	Placebo (211LE201) to BIIB023 3 mg/ kg (211LE202)	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)	7 / 33 (21.21%)	4 / 13 (30.77%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Hepatic enzyme abnormal			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Tension headache			

subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Aphakia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Stevens-johnson syndrome			

subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 13 (0.00%)
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			
Psychotic disorder			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 13 (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
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	0 / 14 (0.00%)	3 / 33 (9.09%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 13 (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
Septic shock			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	0 / 13 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tuberculosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 13 (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
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	0 / 13 (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

Serious adverse events	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 27 (11.11%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Investigations			
Hepatic enzyme abnormal			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Tension headache			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Eye disorders			
Aphakia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cataract			
subjects affected / exposed	0 / 27 (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	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Stevens-johnson syndrome			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Lupus nephritis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

Appendicitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastroenteritis norovirus			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Tuberculosis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 27 (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	Placebo (211LE201) to BIIB023 3 mg/ kg (211LE202)	BIIB023 3 mg/kg (211LE201) to BIIB023 3 mg/kg (211LE202)	Placebo (211LE201) to BIIB023 20 mg/kg (211LE202)
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 14 (28.57%)	19 / 33 (57.58%)	7 / 13 (53.85%)
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	2 / 33 (6.06%) 3	0 / 13 (0.00%) 0
General disorders and administration site conditions Face oedema subjects affected / exposed occurrences (all) Oedema subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0 1 / 14 (7.14%) 2 0 / 14 (0.00%) 0	0 / 33 (0.00%) 0 1 / 33 (3.03%) 1 2 / 33 (6.06%) 2	1 / 13 (7.69%) 2 0 / 13 (0.00%) 0 0 / 13 (0.00%) 0
Reproductive system and breast disorders Menopausal symptoms subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2 0 / 14 (0.00%) 0	1 / 33 (3.03%) 1 3 / 33 (9.09%) 3	0 / 13 (0.00%) 0 0 / 13 (0.00%) 0
Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) Gamma-glutamyltransferase increased	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	0 / 13 (0.00%) 0

subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 33 (3.03%) 1	0 / 13 (0.00%) 0
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	3 / 33 (9.09%) 3	0 / 13 (0.00%) 0
Red blood cell count decreased subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Spleen palpable subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Transaminases increased subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	0 / 13 (0.00%) 0
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Foot fracture subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 33 (3.03%) 1	0 / 13 (0.00%) 0
Road traffic accident subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Nervous system disorders			
Dysgeusia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Headache subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 33 (3.03%) 1	4 / 13 (30.77%) 4
Post herpetic neuralgia			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2	0 / 33 (0.00%) 0	0 / 13 (0.00%) 0
Tension headache subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 33 (3.03%) 1	2 / 13 (15.38%) 2
Constipation subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 33 (3.03%) 1	1 / 13 (7.69%) 1
Gastritis subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	2 / 33 (6.06%) 2	0 / 13 (0.00%) 0
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	2 / 33 (6.06%) 2	1 / 13 (7.69%) 5
Nausea subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Granulomatous liver disease subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Hypertransaminaemia			

subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Skin and subcutaneous tissue disorders			
Butterfly rash			
subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Dermatitis			
subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 33 (0.00%) 0	0 / 13 (0.00%) 0
Livedo reticularis			
subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Rash			
subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 33 (3.03%) 1	1 / 13 (7.69%) 1
Rash pruritic			
subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Systemic lupus erythematosus rash			
subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 33 (0.00%) 0	0 / 13 (0.00%) 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Dysuria			
subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 2
Renal impairment			
subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 33 (0.00%) 0	1 / 13 (7.69%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	3 / 33 (9.09%) 3	0 / 13 (0.00%) 0
Arthritis			

subjects affected / exposed	0 / 14 (0.00%)	1 / 33 (3.03%)	1 / 13 (7.69%)
occurrences (all)	0	1	2
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	2 / 13 (15.38%)
occurrences (all)	0	0	2
Osteoporosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 14 (7.14%)	5 / 33 (15.15%)	0 / 13 (0.00%)
occurrences (all)	1	5	0
Gastroenteritis norovirus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Herpes zoster			
subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	2 / 33 (6.06%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 33 (3.03%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Onychomycosis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 33 (6.06%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Oral herpes			
subjects affected / exposed	0 / 14 (0.00%)	2 / 33 (6.06%)	0 / 13 (0.00%)
occurrences (all)	0	6	0

Pharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	5 / 33 (15.15%)	0 / 13 (0.00%)
occurrences (all)	1	8	0
Urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	2 / 33 (6.06%)	4 / 13 (30.77%)
occurrences (all)	0	2	5
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	2 / 33 (6.06%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 33 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hyperlipidaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 33 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	BIIB023 20 mg/kg (211LE201) to BIIB023 20 mg/kg (211LE202)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 27 (48.15%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Oedema peripheral			

subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Reproductive system and breast disorders Menopausal symptoms subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0 0 / 27 (0.00%) 0		
Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) Haemoglobin decreased subjects affected / exposed occurrences (all) Hepatic enzyme increased subjects affected / exposed occurrences (all) Red blood cell count decreased subjects affected / exposed occurrences (all) Spleen palpable subjects affected / exposed occurrences (all) Transaminases increased subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2 2 / 27 (7.41%) 2 0 / 27 (0.00%) 0 1 / 27 (3.70%) 2 0 / 27 (0.00%) 0 0 / 27 (0.00%) 0 2 / 27 (7.41%) 2		

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Foot fracture			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Road traffic accident			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	3		
Post herpetic neuralgia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Tension headache			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Diarrhoea			

subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Gastritis subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Granulomatous liver disease subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Hypertransaminaemia subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Skin and subcutaneous tissue disorders Butterfly rash subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Dermatitis subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Livedo reticularis subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Rash pruritic			

<p>subjects affected / exposed occurrences (all)</p> <p>Systemic lupus erythematosus rash subjects affected / exposed occurrences (all)</p>	<p>0 / 27 (0.00%) 0</p> <p>0 / 27 (0.00%) 0</p>		
<p>Renal and urinary disorders</p> <p>Acute kidney injury subjects affected / exposed occurrences (all)</p> <p>Dysuria subjects affected / exposed occurrences (all)</p> <p>Renal impairment subjects affected / exposed occurrences (all)</p>	<p>0 / 27 (0.00%) 0</p> <p>2 / 27 (7.41%) 2</p> <p>0 / 27 (0.00%) 0</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia subjects affected / exposed occurrences (all)</p> <p>Arthritis subjects affected / exposed occurrences (all)</p> <p>Back pain subjects affected / exposed occurrences (all)</p> <p>Muscle spasms subjects affected / exposed occurrences (all)</p> <p>Osteoporosis subjects affected / exposed occurrences (all)</p> <p>Pain in extremity subjects affected / exposed occurrences (all)</p>	<p>1 / 27 (3.70%) 4</p> <p>0 / 27 (0.00%) 0</p> <p>1 / 27 (3.70%) 1</p> <p>0 / 27 (0.00%) 0</p> <p>0 / 27 (0.00%) 0</p> <p>2 / 27 (7.41%) 3</p>		
<p>Infections and infestations</p>			

Bronchitis			
subjects affected / exposed	5 / 27 (18.52%)		
occurrences (all)	7		
Gastroenteritis norovirus			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences (all)	2		
Onychomycosis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperkalaemia			

subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Hyperlipidaemia			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		

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? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study was terminated based on a pre-specified, blinded futility analysis of Study 211LE201 (2011-002159-32), which didn't demonstrate sufficient efficacy to warrant continuation of the studies. Study was not terminated based on safety considerations.

Notes: