Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of BIIB023 in Subjects With Lupus Nephritis

Summary

EudraCT number	2011-002159-32
Trial protocol	PT BE DE ES HU IT PL
Global end of trial date	09 December 2015

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	211LE201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01499355
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	09 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 December 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the efficacy of BIIB023 as an add-on treatment to background therapy compared with placebo in combination with background therapy in the treatment of subjects with active, biopsy-proven lupus nephritis. The secondary objectives of this study are to assess the safety and tolerability of BIIB023 compared with placebo in this study population.

Subjects who completed this study through Week 52 were offered the option to enter an extension study under a separate protocol 211LE202 (2013-000594-69).

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:

Oral corticosteroids (prednisone or equivalent) at a target prednisone dose of 10 mg/day. Mycophenolate mofetil (MMF) titrated to a target dose of 2 g/day (1 g twice daily).

Evidence for comparator: -

Actual start date of recruitment	27 July 2012
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: 54
Country: Number of subjects enrolled	Malaysia: 29
Country: Number of subjects enrolled	United States: 27
Country: Number of subjects enrolled	Philippines: 24
Country: Number of subjects enrolled	Peru: 23
Country: Number of subjects enrolled	Mexico: 18
Country: Number of subjects enrolled	Thailand: 16
Country: Number of subjects enrolled	Colombia: 14
Country: Number of subjects enrolled	Brazil: 9
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Hong Kong: 8
Country: Number of subjects enrolled	France: 7

Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Russian Federation: 2
Country: Number of subjects enrolled	Serbia: 2
Country: Number of subjects enrolled	Spain: 2
Worldwide total number of subjects	276
EEA total number of subjects	40

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)	276
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 276 subjects were enrolled and 203 completed the run-in period and qualified for randomization; of these, 15 subjects were not randomized.

Period 1

Period 1 title	Run-In Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All Enrolled Subjects

Arm description:

At Run-in Day 1, subjects entering the study received oral corticosteroid (prednisone or equivalent) starting at 0.75 mg/kg/day (maximum allowed dose of 60 mg/day) for 2 weeks and subsequently tapered over an 8-week period to 10 mg/day by Run-in Week 10. Following confirmation of eligibility, subjects also received MMF starting at Run-in Day 1 at a total dose of 1 g/day and titrated to a target dose of 2 g/day by Run-in Week 2.

Arm type	run-in period (background therapy)
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:

At Run-in Day 1, subjects entering the study received oral corticosteroid (prednisone or equivalent) starting at 0.75 mg/kg/day (maximum allowed dose of 60 mg/day) for 2 weeks and subsequently tapered over an 8-week period to 10 mg/day by Run-in Week 10.

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:

Following confirmation of eligibility, subjects also received MMF starting at Run-in Day 1 at a total dose of 1 g/day and titrated to a target dose of 2 g/day by Run-in Week 2. Subjects already receiving MMF prior to Screening, but at a dose of <2 g/day, were to have their dose titrated up to the target daily dose by Run-in Week 2. The MMF dose could be titrated up to a maximum dose of 3 g/day at the Investigator’s discretion.

Number of subjects in period 1	All Enrolled Subjects
Started	276
Completed	245
Not completed	31
Adverse Event	8
Study Termination	15
Death	2
Not Specified	3
Investigator Decision	2
Consent Withdrawn	1

Period 2

Period 2 title	Double-Blind Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

The subject and all study site staff will be blinded to the subject treatment assignments (BIIB023 20 mg/kg, BIIB023 3 mg/kg, or placebo) with the exception of the unblinded Pharmacist or designee who is responsible for preparing the study treatments and the unblinded Pharmacy Monitor.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo intravenous (IV) infusion on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Arm type	Placebo
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:

10 mg/day prednisone dose (or equivalent)

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:

Target dose of 2 g/day (could be titrated up to a maximum dose of 3 g/day at the Investigator’s discretion).

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	sterile normal saline (0.9% sodium chloride for injection)
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects will receive administration of placebo at 14 study visits (Day 1 [Baseline], Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48).

Arm title	BIIB023 3 mg/kg

Arm description:

BIIB023 3 mg/kg IV on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Arm type	Experimental
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:

10 mg/day prednisone dose (or equivalent)

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:

Target dose of 2 g/day (could be titrated up to a maximum dose of 3 g/day at the Investigator’s discretion).

Investigational medicinal product name	BIIB023
Investigational medicinal product code	BIIB023
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received administration of BIIB023 at 14 study visits (Day 1 [Baseline], Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48).

Arm title	BIIB023 20 mg/kg

Arm description:

BIIB023 20 mg/kg IV on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Arm type	Experimental
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:

10 mg/day prednisone dose (or equivalent)

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:

Target dose of 2 g/day (could be titrated up to a maximum dose of 3 g/day at the Investigator's discretion).

Investigational medicinal product name	BIIB023
Investigational medicinal product code	BIIB023
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received administration of BIIB023 at 14 study visits (Day 1 [Baseline], Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48).

Number of subjects in period 2[1]	Placebo	BIIB023 3 mg/kg	BIIB023 20 mg/kg
Started	63	63	62
Completed	40	38	39
Not completed	23	25	23
Adverse event, serious fatal	1	-	-
Study Termination	18	16	14
Adverse event, non-fatal	2	3	2
NotSpecified	1	2	2
Investigator Decision	-	3	3
Lost to follow-up	1	-	-
Consent Withdrawn	-	1	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: A total of 276 subjects were enrolled and 203 completed the run-in period and qualified for randomization; of these, 15 subjects were not randomized into Period 2.

Baseline characteristics

Reporting groups	
Reporting group title	All Enrolled Subjects

Reporting group description:

At Run-in Day 1, subjects entering the study received oral corticosteroid (prednisone or equivalent) starting at 0.75 mg/kg/day (maximum allowed dose of 60 mg/day) for 2 weeks and subsequently tapered over an 8-week period to 10 mg/day by Run-in Week 10. Following confirmation of eligibility, subjects also received MMF starting at Run-in Day 1 at a total dose of 1 g/day and titrated to a target dose of 2 g/day by Run-in Week 2.

Reporting group values	All Enrolled Subjects	Total	
Number of subjects	276	276	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	276	276	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	32.3		
standard deviation	± 10.11	-	
Gender, Male/Female			
Units: participants			
Female	242	242	
Male	34	34	

End points

End points reporting groups

Reporting group title	All Enrolled Subjects

Reporting group description:

At Run-in Day 1, subjects entering the study received oral corticosteroid (prednisone or equivalent) starting at 0.75 mg/kg/day (maximum allowed dose of 60 mg/day) for 2 weeks and subsequently tapered over an 8-week period to 10 mg/day by Run-in Week 10. Following confirmation of eligibility, subjects also received MMF starting at Run-in Day 1 at a total dose of 1 g/day and titrated to a target dose of 2 g/day by Run-in Week 2.

Reporting group title	Placebo

Reporting group description:

Placebo intravenous (IV) infusion on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Reporting group title	BIIB023 3 mg/kg

Reporting group description:

BIIB023 3 mg/kg IV on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Reporting group title	BIIB023 20 mg/kg

Reporting group description:

BIIB023 20 mg/kg IV on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Subject analysis set title	mITT: Placebo
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects in the Placebo arm in the mITT population (subjects in ITT population except for those who withdrew from study due to study early termination. (Includes subjects who completed Week 44 infusion and Visits at Week 52/early withdrawal and Week 56/End of Study but withdrew due to study early termination.)

Subject analysis set title	mITT: BIIB023 3 mg/kg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects in the BIIB023 3 mg/kg arm in the mITT population (subjects in ITT population except for those who withdrew from study due to study early termination. (Includes subjects who completed Week 44 infusion and Visits at Week 52/early withdrawal and Week 56/End of Study but withdrew due to study early termination.)

Subject analysis set title	mITT: BIIB023 20 mg/kg
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects in the BIIB023 20 mg/kg arm in the mITT population (subjects in ITT population except for those who withdrew from study due to study early termination. (Includes subjects who completed Week 44 infusion and Visits at Week 52/early withdrawal and Week 56/End of Study but withdrew due to study early termination.)

Subject analysis set title	ITT: Placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the Placebo arm who were randomized and received at least 1 dose of study treatment (placebo).

Subject analysis set title	ITT: BIIB023 3 mg/kg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the Placebo arm who were randomized and received at least 1 dose of study treatment (BIIB023).

Subject analysis set title	ITT: BIIB023 20 mg/kg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the BIIB023 20 mg/kg arm who were randomized and received at least 1 dose of study treatment (BIIB023).

Primary: Percentage of Subjects Who Achieve a Complete or Partial Renal Response at Week 52

End point title	Percentage of Subjects Who Achieve a Complete or Partial Renal Response at Week 52[1]

End point description:

Complete renal response is defined as: (1) urinary protein:creatinine ratio (uPCR) < 0.5 mg/mg with ≥ 50% reduction of uPCR from Day 1 (Baseline; from a 24 hour urine collection); and (2) estimated glomerular filtration rate (eGFR) within normal range. Partial renal response is defined as: (1) ≥ 50% reduction in uPCR from Day 1 (Baseline; from a 24-hour urine collection) and, (2) with one of the following: (a) uPCR of < 1.0 mg/mg if the Day 1 (Baseline) was ≤ 3.0 mg/mg, or, (b) uPCR < 3.0 mg/mg if the Day 1 (Baseline) ratio was > 3.0 mg/mg; and stabilization of renal function (eGFR + or - 25% of Day 1 [Baseline] or serum creatinine within normal range).

End point type	Primary

End point timeframe:

Week 52

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	mITT: Placebo	mITT: BIIB023 3 mg/kg	mITT: BIIB023 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	48	49	48	
Units: percentage of subjects				
number (confidence interval 90%)	25 (14.7 to 35.3)	16 (7.6 to 25)	31 (20.3 to 42.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieve Complete Renal Response at Week 52

End point title	Percentage of Subjects Who Achieve Complete Renal Response at Week 52

End point description:

Complete renal response is defined as uPCR < 0.5 mg/mg with ≥ 50% reduction of uPCR from Baseline (from a 24-hour urine collection) and eGFR within normal range.

End point type	Secondary

End point timeframe:

Week 52

End point values	mITT: Placebo	mITT: BIIB023 3 mg/kg	mITT: BIIB023 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	48	49	48	
Units: percentage of subjects				
number (not applicable)	6	8	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Renal Response (Partial or Complete) in Subjects Who Achieve Renal Response at Week 52

End point title	Time to Renal Response (Partial or Complete) in Subjects Who Achieve Renal Response at Week 52

End point description:

Onset of renal response was calculated as weeks elapsed from baseline date to first visit where renal response was achieved. Complete renal response is defined as: (1) uPCR <0.5 mg/mg with ≥ 50% reduction of uPCR from Day 1 (Baseline) (from a 24 hour urine collection); and (2) eGFR within normal range. Partial renal response is defined as: (1) ≥ 50% reduction in uPCR from Day 1 (Baseline; from a 24-hour urine collection) and, (2) with one of the following: (a) uPCR of < 1.0 mg/mg if the Day 1 (Baseline) was ≤ 3.0 mg/mg, or, (b) uPCR < 3.0 mg/mg if the Day 1 (Baseline) ratio was > 3.0 mg/mg; and stabilization of renal function (eGFR + or - 25% of Day 1 [Baseline] or serum creatinine within normal range). Estimated from the Kaplan-Meier Curve.

End point type	Secondary

End point timeframe:

Baseline to Week 52

End point values	ITT: Placebo	ITT: BIIB023 3 mg/kg	ITT: BIIB023 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[2]	8[3]	15[4]	
Units: weeks				
median (full range (min-max))	10.6 (2 to 41)	5.2 (2 to 28)	4.1 (2 to 37)	

Notes:

[2] - Subjects who achieved a renal response at Week 52.

[3] - Subjects who achieved a renal response at Week 52.

[4] - Subjects who achieved a renal response at Week 52.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ITT: Placebo v ITT: BIIB023 3 mg/kg
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.367 [5]
Method	Cox proportional hazard

Notes:

[5] - P-Value from Cox proportional hazard model, including the variable for treatment, adjusted for the covariates including region (Latin America, Asia, rest of world [ROW]) and renal response at Run-in Week 12 (partial and non-response).

Statistical analysis title	Statistical Analysis 2
Comparison groups	ITT: Placebo v ITT: BIIB023 20 mg/kg
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.283 [6]
Method	Cox proportional hazard

Notes:

[6] - P-Value from Cox proportional hazard model, including the variable for treatment, adjusted for the covariates
including region (Latin America, Asia, ROW) and renal response at Run-in Week 12 (partial and non-response).

Secondary: Duration of Renal Response in Participants Who Achieve Partial or Complete Renal Response at Any Time During the Study

End point title	Duration of Renal Response in Participants Who Achieve Partial or Complete Renal Response at Any Time During the Study

End point description:

Number of days between first visit with response to last consecutive visit with partial or complete response. Complete renal response is defined as: (1) uPCR <0.5 mg/mg with ≥ 50% reduction of uPCR from Day 1 (Baseline) (from a 24 hour urine collection); and (2) eGFR within normal range. Partial renal response is defined as: (1) ≥ 50% reduction in uPCR from Day 1 (Baseline; from a 24-hour urine collection) and, (2) with one of the following: (a) uPCR of < 1.0 mg/mg if the Day 1 (Baseline) was ≤ 3.0 mg/mg, or, (b) uPCR < 3.0 mg/mg if the Day 1 (Baseline) ratio was > 3.0 mg/mg; and stabilization of renal function (eGFR + or - 25% of Day 1 [Baseline] or serum creatinine within normal range). Estimated from the Kaplan-Meier Curve.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	ITT: Placebo	ITT: BIIB023 3 mg/kg	ITT: BIIB023 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	48	39	40	
Units: days				
arithmetic mean (standard deviation)	48.3 (± 83.23)	45.6 (± 75.42)	52.1 (± 106.72)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	ITT: Placebo v ITT: BIIB023 3 mg/kg

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.863
Method	Regression, Cox

Statistical analysis title	Statistical Analysis 2
Comparison groups	ITT: Placebo v ITT: BIIB023 20 mg/kg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.769
Method	Regression, Cox

Statistical analysis title	Statistical Analysis 3
Comparison groups	ITT: Placebo v ITT: BIIB023 3 mg/kg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.907
Method	ANCOVA

Statistical analysis title	Statistical Analysis 4
Comparison groups	ITT: Placebo v ITT: BIIB023 20 mg/kg
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.996
Method	ANCOVA

Secondary: Percentage of Subjects With uPCR > 3.0 mg/mg at Baseline Who Achieve uPCR <1.0 mg/mg at Week 52

End point title	Percentage of Subjects With uPCR > 3.0 mg/mg at Baseline Who Achieve uPCR <1.0 mg/mg at Week 52

End point description:

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 52

End point values	mITT: Placebo	mITT: BIIB023 3 mg/kg	mITT: BIIB023 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12[7]	18[8]	15[9]	
Units: percentage of subjects				
number (not applicable)	0	22	13	

Notes:

[7] - Subjects with a uPCR > 3.0 mg/mg at Baseline

[8] - Subjects with a uPCR > 3.0 mg/mg at Baseline

[9] - Subjects with a uPCR > 3.0 mg/mg at Baseline

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	mITT: BIIB023 3 mg/kg v mITT: Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0486 [10]
Method	Cochran-Mantel-Haenszel

Notes:

[10] - Model includes the variable for treatment, adjusted for the covariates including region (Latin America, Asia, ROW) and renal response at Run-in Week 12 (partial and non-response).

Statistical analysis title	Statistical Analysis 2
Comparison groups	mITT: Placebo v mITT: BIIB023 20 mg/kg
Number of subjects included in analysis	27
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0668 [11]
Method	Cochran-Mantel-Haenszel

Notes:

[11] - Model includes the variable for treatment, adjusted for the covariates including region (Latin America, Asia, ROW) and renal response at Run-in Week 12 (partial and non-response).

Secondary: Percentage of Subjects With Active Urinary Sediment at Baseline Who Have Inactive Urinary Sediment at Week 52

End point title	Percentage of Subjects With Active Urinary Sediment at Baseline Who Have Inactive Urinary Sediment at Week 52

End point description:

Active urinary sediment is defined by 1 of the following (in the absence of a urinary tract infection or menses): > 5 red blood cell/high power field (RBC/HPF) or above the reference range for the laboratory, and > 5 white blood cell/high power field (WBC/HPF) or above the reference range for the laboratory, and presence of cellular casts (RBC or WBC). Inactive urinary sediment is defined as: < 5 RBC/HPF and < 5 WBC/HPF, or within the laboratory reference range, and no cellular casts (no RBC or WBC casts).

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	mITT: Placebo	mITT: BIIB023 3 mg/kg	mITT: BIIB023 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[12]	21[13]	14[14]	
Units: percentage of subjects				
number (confidence interval 90%)	38 (17.6 to 57.4)	5 (0 to 12.4)	21 (3.4 to 39.5)	

Notes:

[12] - Subjects with active urinary sediment at Day 1

[13] - Subjects with active urinary sediment at Day 1

[14] - Subjects with active urinary sediment at Day 1

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	mITT: Placebo v mITT: BIIB023 3 mg/kg
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0456 [15]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.0628
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.0081
upper limit	0.4843

Notes:

[15] - Model includes the variable for treatment, adjusted for the covariates including region (Latin America, Asia, ROW) and renal response at Run-in Week 12 (partial and non-response).

Statistical analysis title	Statistical Analysis 2
Comparison groups	mITT: Placebo v mITT: BIIB023 20 mg/kg
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5455 [16]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.4344
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.0996
upper limit	1.8941

Notes:

[16] - Model includes the variable for treatment, adjusted for the covariates including region (Latin America, Asia, ROW) and renal response at Run-in Week 12 (partial and non-response).

Statistical analysis title	Statistical Analysis 3
Comparison groups	mITT: Placebo v mITT: BIIB023 3 mg/kg
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0252
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical Analysis 4
Comparison groups	mITT: Placebo v mITT: BIIB023 20 mg/kg
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2876
Method	Cochran-Mantel-Haenszel

Secondary: Number of Subjects with Adverse Events (AEs), Serious Adverse Events (SAEs) and AEs Leading to Study Discontinuation During the Run-In Period

End point title	Number of Subjects with Adverse Events (AEs), Serious Adverse Events (SAEs) and AEs Leading to Study Discontinuation During the Run-In Period

End point description:

AEs that had an onset on or after dosing of MMF on run-in Day 1 up to the first double-blind dose, or any pre-existing condition that worsened. 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	Secondary

End point timeframe:

Day 1 to Week 12

End point values	All Enrolled Subjects			
Subject group type	Reporting group			
Number of subjects analysed	276			
Units: subjects				
number (not applicable)				
Any Event	209			
Moderate or Severe Event	94			
Severe Event	18			
Related Event to MMF	90			
Serious Event	28			

Related Serious Event to MMF	12			
Fatal Event	2			
Discontinued Treatment Due to Event	0			
Withdrew From Study Due to Event	10			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with AEs, SAEs and AEs Leading to Study Discontinuation During the Double-Blind Period

End point title	Number of Subjects with AEs, SAEs and AEs Leading to Study Discontinuation During the Double-Blind Period

End point description:

AEs that had an onset on or after dosing of BIIB023 or placebo, or any pre-existing condition that worsened. 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	Secondary

End point timeframe:

Week 12 to Week 56

End point values	Placebo	BIIB023 3 mg/kg	BIIB023 20 mg/kg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	63	62	
Units: subjects				
number (not applicable)				
Any event	48	60	53	
Moderate or severe event	26	32	22	
Severe event	4	6	5	
Event related to double-blind treatment	5	15	11	
Event related to MMF	21	24	22	
Serious event	7	11	10	
Serious event related to double-blind treatment	3	3	2	
Serious event related to MMF	6	4	3	
Fatal event	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Renal Response in Subjects Who Achieve Complete Renal Response at Week 52

End point title	Duration of Renal Response in Subjects Who Achieve Complete Renal Response at Week 52

End point description:

Duration of response was calculated as the days in between the date of Week 52 visit and the date when the participant last became complete renal responder on or before Week 52 visit. Complete renal response: (1) uPCR <0.5 mg/mg with ≥ 50% reduction of uPCR from Day 1 (Baseline) (from a 24 hour urine collection); and (2) eGFR within normal range.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	mITT: Placebo	mITT: BIIB023 3 mg/kg	mITT: BIIB023 20 mg/kg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	48	49	49	
Units: subjects				
1-day duration	2	3	2	
27-day duration	0	0	1	
78-day duration	0	1	0	
141-day duration	1	0	0	
169-day duration	0	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs: Run-in Day 1 through Week 64 +/- 5 days. SAEs: Screening through Week 64 +/- 5 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Run-in period

Reporting group description:

At Run-in Day 1, subjects entering the study received oral corticosteroid (prednisone or equivalent) starting at 0.75 mg/kg/day (maximum allowed dose of 60 mg/day) for 2 weeks and subsequently tapered over an 8-week period to 10 mg/day by Run-in Week 10. Following confirmation of eligibility, subjects also received MMF starting at Run-in Day 1 at a total dose of 1 g/day and titrated to a target dose of 2 g/day by Run-in Week 2.

Reporting group title	Placebo

Reporting group description:

Placebo IV infusion on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Reporting group title	BIIB023 3mg/kg

Reporting group description:

BIIB023 3 mg/kg IV on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Reporting group title	BIIB023 20 mg/kg

Reporting group description:

BIIB023 20 mg/kg IV on Day 1, Week 2, Week 4, Week 8, and every 4 weeks thereafter through Week 48, plus background therapy of oral steroids (prednisone or equivalent) and MMF.

Serious adverse events	Run-in period	Placebo	BIIB023 3mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 276 (10.14%)	7 / 63 (11.11%)	11 / 63 (17.46%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (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
Vascular disorders			
Hypotension			

subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Papilloma excision			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
Oedema peripheral			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary congestion			

subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
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			
Transient ischaemic attack			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	2 / 276 (0.72%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 276 (0.72%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
Food poisoning			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (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
Vomiting			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Drug-induced liver injury			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glomerulonephritis rapidly progressive			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
Lupus nephritis			
subjects affected / exposed	2 / 276 (0.72%)	0 / 63 (0.00%)	3 / 63 (4.76%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			

subjects affected / exposed	1 / 276 (0.36%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Brain abscess			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysentery			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (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
Endocarditis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	3 / 63 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	4 / 276 (1.45%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			

subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
Peritonitis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 276 (0.72%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 276 (0.00%)	1 / 63 (1.59%)	0 / 63 (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
Urinary tract infection			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (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
Urosepsis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 276 (0.00%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 63 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BIIB023 20 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 62 (16.13%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Papilloma excision			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Oedema			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary congestion			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congestive cardiomyopathy			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transient ischaemic attack			

subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Faecaloma			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Food poisoning			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Vomiting				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Drug-induced liver injury				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Rash				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Glomerulonephritis rapidly progressive				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lupus nephritis				
subjects affected / exposed	2 / 62 (3.23%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal impairment				

subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Brain abscess			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysentery			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocarditis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Herpes zoster				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 62 (3.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia cytomegaloviral				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 62 (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	Run-in period	Placebo	BIIB023 3mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	134 / 276 (48.55%)	33 / 63 (52.38%)	46 / 63 (73.02%)
Vascular disorders			
Hypertension			
subjects affected / exposed	10 / 276 (3.62%)	0 / 63 (0.00%)	4 / 63 (6.35%)
occurrences (all)	10	0	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 276 (1.09%)	1 / 63 (1.59%)	4 / 63 (6.35%)
occurrences (all)	3	1	5
Headache			
subjects affected / exposed	12 / 276 (4.35%)	6 / 63 (9.52%)	7 / 63 (11.11%)
occurrences (all)	12	10	9
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 276 (2.54%)	4 / 63 (6.35%)	4 / 63 (6.35%)
occurrences (all)	7	4	5
Leukopenia			
subjects affected / exposed	10 / 276 (3.62%)	7 / 63 (11.11%)	5 / 63 (7.94%)
occurrences (all)	10	9	5
Neutropenia			
subjects affected / exposed	3 / 276 (1.09%)	4 / 63 (6.35%)	5 / 63 (7.94%)
occurrences (all)	3	7	5
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	8 / 276 (2.90%)	1 / 63 (1.59%)	4 / 63 (6.35%)
occurrences (all)	11	1	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	31 / 276 (11.23%)	2 / 63 (3.17%)	2 / 63 (3.17%)
occurrences (all)	39	2	3
Nausea			

subjects affected / exposed	14 / 276 (5.07%)	3 / 63 (4.76%)	5 / 63 (7.94%)
occurrences (all)	14	4	5
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	8 / 276 (2.90%)	1 / 63 (1.59%)	5 / 63 (7.94%)
occurrences (all)	8	1	5
Rash			
subjects affected / exposed	8 / 276 (2.90%)	4 / 63 (6.35%)	4 / 63 (6.35%)
occurrences (all)	8	4	4
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 276 (0.36%)	3 / 63 (4.76%)	5 / 63 (7.94%)
occurrences (all)	1	3	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 276 (3.62%)	6 / 63 (9.52%)	6 / 63 (9.52%)
occurrences (all)	11	7	6
Infections and infestations			
Bronchitis			
subjects affected / exposed	10 / 276 (3.62%)	1 / 63 (1.59%)	3 / 63 (4.76%)
occurrences (all)	12	1	3
Gastroenteritis			
subjects affected / exposed	9 / 276 (3.26%)	6 / 63 (9.52%)	6 / 63 (9.52%)
occurrences (all)	11	6	8
Influenza			
subjects affected / exposed	4 / 276 (1.45%)	2 / 63 (3.17%)	1 / 63 (1.59%)
occurrences (all)	4	2	1
Nasopharyngitis			
subjects affected / exposed	13 / 276 (4.71%)	3 / 63 (4.76%)	5 / 63 (7.94%)
occurrences (all)	13	5	5
Upper respiratory tract infection			
subjects affected / exposed	21 / 276 (7.61%)	7 / 63 (11.11%)	13 / 63 (20.63%)
occurrences (all)	24	8	18
Urinary tract infection			
subjects affected / exposed	8 / 276 (2.90%)	2 / 63 (3.17%)	6 / 63 (9.52%)
occurrences (all)	8	2	7

Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	11 / 276 (3.99%) 11	1 / 63 (1.59%) 1	6 / 63 (9.52%) 13

Non-serious adverse events	BIIB023 20 mg/kg		
Total subjects affected by non-serious adverse events subjects affected / exposed	43 / 62 (69.35%)		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	5 / 62 (8.06%) 5		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	3 / 62 (4.84%) 4 6 / 62 (9.68%) 7		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	7 / 62 (11.29%) 7 2 / 62 (3.23%) 2 0 / 62 (0.00%) 0		
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea	8 / 62 (12.90%) 8		

subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 3		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 3 / 62 (4.84%) 3 0 / 62 (0.00%) 0		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	 6 / 62 (9.68%) 7		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 5 / 62 (8.06%) 5		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 7 / 62 (11.29%) 11 7 / 62 (11.29%) 9 4 / 62 (6.45%) 4 5 / 62 (8.06%) 5 6 / 62 (9.68%) 9 2 / 62 (3.23%) 2		

Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	 3 / 62 (4.84%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2011	A global amendment was implemented to: - revise the reproductive toxicity (Segent 2, teratology) section - update Exclusion 3 to change "global fibrosis" to "diffuse fibrosis" - update contraception requirements to require at least 2 methods of birth control, including at least 1 barrier method
18 October 2012	A global amendment was implemented to: - update inclusion criteria to allow renal biopsies to be performed during the Screening Period if no renal biopsy from the last 3 months was available - simplify parameters of proteinuria at Screening (Inclusion Criteria 5) as uPCR > 1.0 mg/mg - increase the contraception requirement from 3 months to 6 months after last dose of study treatment - update tuberculosis exclusion criteria to allow local guidelines to be followed - remove the use of steroids from the exclusion criteria
24 January 2014	A global amendment was implemented to: - add an interim analysis for futility - change the number of subjects to be randomized into the Double-Blind Period from approximately 220 to approximately 210 - change the Screening window from 28 days to 35 days prior to Run-in Day 1, regardless of whether or not a subject had a renal biopsy performed during Screening - allow subjects who had a uPCR <0.5 mg/mg at Run-in (Week 12) and consequently did not meet the Randomization Inclusion Criteria to have the 24-hour uPCR repeated once within 4 weeks prior to Baseline at the Investigator's discretion - revise Exclusion Criterion 18 to include any abnormal laboratory value at Screening considered by the Investigator to be clinically significant - revise Exclusion Criterion 28 to allow subjects taking cyclophosphamide, calcineurin, or a calcineurin inhibitor from within 12 months to within 6 months prior to Screening to be eligible for the study - revise the temporary dose reduction of MMF to <1.5 g/day for >14 days during the Double-Blind Period

Notes:

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 the review of results following the prespecified, blinded futility analysis, which did not demonstrate sufficient efficacy to warrant continuation of the study. Study was not terminated based on safety considerations.

Notes: