Clinical trial results:
A double-blind, randomised, placebo-controlled trial evaluating the effect of BI 655064 administered as subcutaneous injections, on renal response after one year of treatment, in patients with active lupus nephritis

Summary

EudraCT number	2015-001750-15
Trial protocol	ES CZ GR DE PL AT PT GB FR IT
Global end of trial date	18 August 2020

Results information

Result version number	v2 (current)
This version publication date	14 November 2021
First version publication date	04 July 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	1293.10

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02770170
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.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 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 June 2020
Global end of trial reached?	Yes
Global end of trial date	18 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives were to characterise the dose-response relationship, identify the target dose for Phase III development, and investigate the safety and efficacy of 3 doses of BI 655064 administered subcutaneously for 52 weeks as add-on therapy to standard of care treatment in patients with active lupus nephritis.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct. Rescue medication was allowed for all patients as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 August 2016
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	Australia: 2
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Czechia: 6
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Japan: 15
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Mexico: 22
Country: Number of subjects enrolled	Philippines: 28
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Portugal: 7
Country: Number of subjects enrolled	Serbia: 7
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Thailand: 26
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 31
Country: Number of subjects enrolled	Korea, Republic of: 3

Worldwide total number of subjects	209
EEA total number of subjects	62

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)	207
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This is a double-blind, randomised, placebo-controlled trial evaluating the effect of BI 655064 administered as subcutaneous injections, on renal response after one year of treatment, in patients with active lupus nephritis.

Pre-assignment

Screening details:

All patients were screened for eligibility prior to participation in the trial. Patients attended a specialist site which ensured that they (the patients) strictly met all inclusion and none of the exclusion criteria. Patients were not to be allocated to a treatment group if any of the entry criteria were violated.

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

Blinding implementation details:

Double-blind

Arms

Are arms mutually exclusive?	Yes
Arm title	120 mg BI 655064

Arm description:

Participants in dose group 1 received two subcutaneous injections per week, one of 120 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064 alternating with placebo, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	BI 655064
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants in dose group 1 received two subcutaneous injections per week, one of 120 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064 alternating with placebo, up to 52 weeks.

Arm title	180 mg BI 655064

Arm description:

Participants in dose group 2 received two subcutaneous injections per week, one of 180 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 180 mg of BI 655064 alternating with placebo, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	BI 655064
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants in dose group 2 received two subcutaneous injections per week, one of 180 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 180 mg of BI 655064 alternating with placebo, up to 52 weeks.

Arm title	240 mg BI 655064

Arm description:

Participants in dose group 3 received two subcutaneous injections per week of 120 milligrams (mg) of BI 655064 (240 mg in total) on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064, up to 52 weeks.

Arm type	Experimental
Investigational medicinal product name	BI 655064
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants in dose group 3 received two subcutaneous injections per week of 120 milligrams (mg) of BI 655064 (240 mg in total) on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064, up to 52 weeks.

Arm title	Placebo

Arm description:

Participants in the placebo group received two subcutaneous injections per week of placebo on the same day for 3 weeks followed by one subcutaneous injection per week of placebo, up to 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants in the placebo group received two subcutaneous injections per week of placebo on the same day for 3 weeks followed by one subcutaneous injection per week of placebo, up to 52 weeks.

Number of subjects in period 1[1]	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064
Started	21	20	40
Completed	14	17	35
Not completed	7	3	5
due to disease worsening	-	-	-
Lack of efficacy	2	-	-
Adverse event, non-fatal	4	3	5
Consent withdrawn by subject	-	-	-
due to pregnancy	1	-	-

Number of subjects in period 1[1]	Placebo
Started	40
Completed	33
Not completed	7
due to disease worsening	1
Lack of efficacy	1

Adverse event, non-fatal	3
Consent withdrawn by subject	2
due to pregnancy	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one dose of the trial medication.

Baseline characteristics

Reporting groups	
Reporting group title	120 mg BI 655064
Reporting group description:	
Participants in dose group 1 received two subcutaneous injections per week, one of 120 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064 alternating with placebo, up to 52 weeks.	
Reporting group title	180 mg BI 655064
Reporting group description:	
Participants in dose group 2 received two subcutaneous injections per week, one of 180 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 180 mg of BI 655064 alternating with placebo, up to 52 weeks.	
Reporting group title	240 mg BI 655064
Reporting group description:	
Participants in dose group 3 received two subcutaneous injections per week of 120 milligrams (mg) of BI 655064 (240 mg in total) on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064, up to 52 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants in the placebo group received two subcutaneous injections per week of placebo on the same day for 3 weeks followed by one subcutaneous injection per week of placebo, up to 52 weeks.	

Reporting group values	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064
Number of subjects	21	20	40
Age categorical			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	21	20	40
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: years			
arithmetic mean	35.9	34.5	34.3
standard deviation	± 11.4	± 9.9	± 10.3
Sex: Female, Male			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: Participants			
Female	16	18	36
Male	5	2	4

Ethnicity (NIH/OMB)			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
Hispanic or Latino	5	4	8
Not Hispanic or Latino	16	16	32
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	9	9	17
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	2
White	9	11	21
More than one race	1	0	0
Unknown or Not Reported	1	0	0
estimated glomerular filtration rate (eGFR) at baseline			
estimated glomerular filtration rate (eGFR) was calculated from serum creatinine. Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: milliLitres /minute /1.73 squaremeter			
arithmetic mean	85.857	99.850	91.125
standard deviation	± 34.268	± 21.109	± 32.673

Reporting group values	Placebo	Total	
Number of subjects	40	121	
Age categorical			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
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)	40	121	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: years			
arithmetic mean	33.9		
standard deviation	± 9.8	-	
Sex: Female, Male			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			

Units: Participants			
Female	38	108	
Male	2	13	
Ethnicity (NIH/OMB)			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
Hispanic or Latino	7	24	
Not Hispanic or Latino	33	97	
Unknown or Not Reported	0	0	
Race (NIH/OMB)			
Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	17	52	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	4	
White	22	63	
More than one race	0	1	
Unknown or Not Reported	0	1	
estimated glomerular filtration rate (eGFR) at baseline			
estimated glomerular filtration rate (eGFR) was calculated from serum creatinine. Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.			
Units: milliLitres /minute /1.73 squaremeter			
arithmetic mean	88.775		
standard deviation	± 29.914	-	

End points

End points reporting groups

Reporting group title	120 mg BI 655064

Reporting group description:

Participants in dose group 1 received two subcutaneous injections per week, one of 120 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064 alternating with placebo, up to 52 weeks.

Reporting group title	180 mg BI 655064

Reporting group description:

Participants in dose group 2 received two subcutaneous injections per week, one of 180 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 180 mg of BI 655064 alternating with placebo, up to 52 weeks.

Reporting group title	240 mg BI 655064

Reporting group description:

Participants in dose group 3 received two subcutaneous injections per week of 120 milligrams (mg) of BI 655064 (240 mg in total) on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064, up to 52 weeks.

Reporting group title	Placebo

Reporting group description:

Participants in the placebo group received two subcutaneous injections per week of placebo on the same day for 3 weeks followed by one subcutaneous injection per week of placebo, up to 52 weeks.

Subject analysis set title	120 mg BI 655064
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants in dose group 1 received two subcutaneous injections per week, one of 120 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064 alternating with placebo, up to 52 weeks.

Subject analysis set title	180 mg BI 655064
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants in dose group 2 received two subcutaneous injections per week, one of 180 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 180 mg of BI 655064 alternating with placebo, up to 52 weeks.

Subject analysis set title	240 mg BI 655064
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants in dose group 3 received two subcutaneous injections per week of 120 milligrams (mg) of BI 655064 (240 mg in total) on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064, up to 52 weeks.

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

Subject analysis set description:

Participants in the placebo group received two subcutaneous injections per week of placebo on the same day for 3 weeks followed by one subcutaneous injection per week of placebo, up to 52 weeks.

Primary: Percentage of patients with complete renal response (CRR) at week 52

End point title	Percentage of patients with complete renal response (CRR) at week 52

End point description:

Complete renal response (CRR) was defined as urine protein (UP) < 0.5 g/day at Week 52 and either estimated glomerular filtration rate (eGFR) within normal range at Week 52 or decrease in eGFR < 20% from baseline at Week 52 if eGFR was below normal range (below lower limit of normal [LLN], where LLN = 90 mL/min).
CRR at Week 52 (derived using UP from the 24 h urine collections) was analyzed using a logistic regression model. Factors in the model included treatment and the covariates race (Asian/Non-Asian)

and proteinuria at screening (UP/urine creatinine (UC) <3 or >=3 g/day).
Pairwise comparisons of the modelled proportions of patients with CRR at each dose level to placebo were performed.
Intent to treat (ITT) set: This patient set included all patients from the treated set who had a baseline (or screening) proteinuria (spot urine could be used if a patient did not have 24 h urine collections) and a baseline or screening estimated glomerular filtration rate (eGFR) value.

End point type	Primary

End point timeframe:

At week 52.

End point values	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	40	40
Units: Percentage of Participants				
number (not applicable)	38.32	44.95	44.56	48.33

Statistical analyses

Statistical analysis title	MCPMod quadratic model fit

Statistical analysis description:

Multiple comparison procedures and modelling (MCPmod) techniques for logistic regression was used.

Comparison groups	120 mg BI 655064 v 180 mg BI 655064 v 240 mg BI 655064 v Placebo
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7271 [1]
Method	MCPMod quadratic model fit

Notes:

[1] - An alpha of 0.20 was used for one-sided test. The MCPMod procedure adjusts for multiplicity.

Statistical analysis title	MCPMod sigmoidal Emax model fit

Statistical analysis description:

Multiple comparison procedures and modelling (MCPmod) techniques for logistic regression was used.

Comparison groups	120 mg BI 655064 v 180 mg BI 655064 v 240 mg BI 655064 v Placebo
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6415 [2]
Method	MCPMod sigmoidal Emax model fit

Notes:

[2] - An alpha of 0.20 was used for one-sided test. The MCPMod procedure adjusts for multiplicity.

Statistical analysis title	MCPMod Emax model fit

Statistical analysis description:

Multiple comparison procedures and modelling (MCPmod) techniques for logistic regression was used.

Comparison groups	120 mg BI 655064 v 180 mg BI 655064 v 240 mg BI 655064 v Placebo
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7367 [3]
Method	MCPMod Emax model fit

Notes:

[3] - An alpha of 0.20 was used for one-sided test. The MCPMod procedure adjusts for multiplicity.

Statistical analysis title	MCPMod exponential model fit

Statistical analysis description:

Multiple comparison procedures and modelling (MCPmod) techniques for logistic regression was used.

Comparison groups	120 mg BI 655064 v 180 mg BI 655064 v 240 mg BI 655064 v Placebo
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6624 [4]
Method	MCPMod exponential model fit

Notes:

[4] - An alpha of 0.20 was used for one-sided test. The MCPMod procedure adjusts for multiplicity.

Statistical analysis title	Logistic regression

Statistical analysis description:

include treatment and covariates, race (Asian or non−Asian), proteinuria at screening (<3g/day or >= 3g/day)
Confidence intervals calculated using delta method

Comparison groups	120 mg BI 655064 v Placebo
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4645
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	-10
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-27.292
upper limit	7.288

Statistical analysis title	Logistic regression

Statistical analysis description:

include treatment and covariates, race (Asian or non−Asian), proteinuria at screening (<3g/day or >= 3g/day)
Confidence intervals calculated using delta method

Comparison groups	180 mg BI 655064 v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified

Analysis type	other
P-value	= 0.8084
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	-3.38
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-21.204
upper limit	14.451

Statistical analysis title	Logistic regression

Statistical analysis description:

include treatment and covariates, race (Asian or non−Asian), proteinuria at screening (<3g/day or >= 3g/day)
Confidence intervals calculated using delta method

Comparison groups	240 mg BI 655064 v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7398
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	-3.77
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-18.364
upper limit	10.832

Secondary: Percentage of patients with complete renal response (CRR) at week 26

End point title	Percentage of patients with complete renal response (CRR) at week 26

End point description:

Complete renal response (CRR) was defined as urine protein (UP) < 0.5 g/day at Week 26 and either estimated glomerular filtration rate (eGFR) within normal range at Week 26 or decrease in eGFR < 20% from baseline at Week 26 if eGFR was below normal range (below lower limit of normal [LLN], where LLN = 90 mL/min).

Intent to treat (ITT) set: This patient set included all patients from the treated set who had a baseline (or screening) proteinuria (spot urine could be used if a patient did not have 24 h urine collections) and a baseline or screening estimated glomerular filtration rate (eGFR) value.

End point type	Secondary

End point timeframe:

At week 26.

End point values	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	40	40
Units: Percentage of Participants				
number (not applicable)	28.6	50.0	35.0	37.5

Statistical analyses

Statistical analysis title	Barnard test of association
Statistical analysis description: Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	120 mg BI 655064 v Placebo
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5773
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	-8.93
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-23.66
upper limit	7.64

Statistical analysis title	Barnard test of association
Statistical analysis description: Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	180 mg BI 655064 v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4013
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	12.5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-4.59
upper limit	29.03

Statistical analysis title	Barnard test of association

Statistical analysis description:	
Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	240 mg BI 655064 v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8965
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	-2.5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-15.98
upper limit	11.1

Secondary: Percentage of patients with partial renal response (PRR) at week 26

End point title	Percentage of patients with partial renal response (PRR) at week 26

End point description:

Partial renal response (PRR) was defined as at least 50% reduction of proteinuria from baseline if estimated glomerular filtration rate (eGFR) was within normal range at time of assessment or decrease of eGFR <20% from baseline if eGFR was below normal range at time of assessment.

Intent to treat (ITT) set: This patient set included all patients from the treated set who had a baseline (or screening) proteinuria (spot urine could be used if a patient did not have 24 h urine collections) and a baseline or screening estimated glomerular filtration rate (eGFR) value.

End point type	Secondary

End point timeframe:

At week 26.

End point values	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	40	40
Units: Percentage of Participants				
number (not applicable)	42.9	75.0	62.5	62.5

Statistical analyses

Statistical analysis title	Barnard test of association
Statistical analysis description:	
Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	120 mg BI 655064 v Placebo
Number of subjects included in analysis	61
Analysis specification	Pre-specified

Analysis type	other
P-value	= 0.1476
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	-19.64
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-35.38
upper limit	-2.48

Statistical analysis title	Barnard test of association
Statistical analysis description:	
Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	240 mg BI 655064 v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	0
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-13.63
upper limit	13.63

Statistical analysis title	Barnard test of association
Statistical analysis description:	
Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	180 mg BI 655064 v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4013
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	12.5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-4.2
upper limit	26.86

Secondary: Percentage of patients with partial renal response (PRR) at week 52	
End point title	Percentage of patients with partial renal response (PRR) at week 52

End point description:

Partial renal response (PRR) was defined as at least 50% reduction of proteinuria from baseline if estimated glomerular filtration rate (eGFR) was within normal range at time of assessment or decrease of eGFR <20% from baseline if eGFR was below normal range at time of assessment.

Intent to treat (ITT) set: This patient set included all patients from the treated set who had a baseline (or screening) proteinuria (spot urine could be used if a patient did not have 24 h urine collections) and a baseline or screening estimated glomerular filtration rate (eGFR) value.

End point type	Secondary

End point timeframe:

At week 52.

End point values	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	40	40
Units: Percentage of Participants				
number (not applicable)	33.3	65.0	55.0	60.0

Statistical analyses

Statistical analysis title	Barnard test of association

Statistical analysis description:

Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method

Comparison groups	120 mg BI 655064 v Placebo
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0512
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	-26.67
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-41.52
upper limit	-9.42

Statistical analysis title	Barnard test of association

Statistical analysis description:

Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method

Comparison groups	180 mg BI 655064 v Placebo
Number of subjects included in analysis	60

Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7597
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-12.1
upper limit	20.74

Statistical analysis title	Barnard test of association
Statistical analysis description:	
Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	240 mg BI 655064 v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7505
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	-5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-18.74
upper limit	9.02

Secondary: Percentage of patients with major renal response (MRR) at week 26

End point title	Percentage of patients with major renal response (MRR) at week 26

End point description:

Major renal response was defined as follows depending on proteinuria at baseline:
-If baseline proteinuria was <3 g/day and patient had complete renal response (CRR)
-If baseline proteinuria was >= 3 g/day and proteinuria < 1 g/day and either estimated glomerular filtration rate (eGFR) within normal range or decrease in eGFR <20% from baseline at Week 26 if eGFR was below normal range (below lower limit of normal (LLN), where LLN = 90 mL/min)

Intent to treat (ITT) set: This patient set included all patients from the treated set who had a baseline (or screening) proteinuria (spot urine could be used if a patient did not have 24 h urine collections) and a baseline or screening estimated glomerular filtration rate (eGFR) value.

End point type	Secondary

End point timeframe:

At week 26.

End point values	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	40	40
Units: Percentage of Participants				
number (not applicable)	28.6	55.0	37.5	50.0

Statistical analyses

Statistical analysis title	Barnard test of association
Statistical analysis description: Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	120 mg BI 655064 v Placebo
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1269
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	-21.43
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-36.03
upper limit	-4.41

Statistical analysis title	Barnard test of association
Statistical analysis description: Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	180 mg BI 655064 v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7889
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-12.24
upper limit	21.62

Statistical analysis title	Barnard test of association

Statistical analysis description:	
Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	240 mg BI 655064 v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2906
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	-12.5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-25.99
upper limit	1.68

Secondary: Percentage of patients with major renal response (MRR) at week 52

End point title	Percentage of patients with major renal response (MRR) at week 52

End point description:

Major renal response was defined as follows depending on proteinuria at baseline:
-If baseline proteinuria was <3 g/day and patient had complete renal response (CRR)
-If baseline proteinuria was >= 3 g/day and proteinuria < 1 g/day and either estimated glomerular filtration rate (eGFR) within normal range or decrease in eGFR <20% from baseline at Week 52 if eGFR was below normal range (below lower limit of normal (LLN), where LLN = 90 mL/min)

Intent to treat (ITT) set: This patient set included all patients from the treated set who had a baseline (or screening) proteinuria (spot urine could be used if a patient did not have 24 h urine collections) and a baseline or screening estimated glomerular filtration rate (eGFR) value.

End point type	Secondary

End point timeframe:

At week 52.

End point values	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	40	40
Units: Percentage of Participants				
number (not applicable)	42.9	55.0	52.5	52.5

Statistical analyses

Statistical analysis title	Barnard test of association

Statistical analysis description:

Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method

Comparison groups	120 mg BI 655064 v Placebo
Number of subjects included in analysis	61

Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5687
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	-9.64
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-25.79
upper limit	7.45

Statistical analysis title	Barnard test of association
Statistical analysis description:	
Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	240 mg BI 655064 v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	0
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-14.03
upper limit	14.03

Statistical analysis title	Barnard test of association
Statistical analysis description:	
Unadjusted absolute risk difference; Confidence intervals calculated using Newcombe method	
Comparison groups	180 mg BI 655064 v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9217
Method	Barnard test of association
Parameter estimate	Risk difference (RD)
Point estimate	2.5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-14.67
upper limit	19.17

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first does of study medication until end of the 52-week treatment + 8 weeks of follow-up, up to 60 weeks.

Adverse event reporting additional description:

Treated set (TS): This patient set included all patients who were dispensed study medication and were documented to have taken at least one dose of investigational treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	120 mg BI 655064

Reporting group description:

Participants in dose group 1 received two subcutaneous injections per week, one of 120 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064 alternating with placebo, up to 52 weeks.

Reporting group title	180 mg BI 655064

Reporting group description:

Participants in dose group 2 received two subcutaneous injections per week, one of 180 milligrams (mg) of BI 655064 and one of matching placebo on the same day for 3 weeks followed by one subcutaneous injection per week of 180 mg of BI 655064 alternating with placebo, up to 52 weeks.

Reporting group title	240 mg BI 655064

Reporting group description:

Participants in dose group 3 received two subcutaneous injections per week of 120 milligrams (mg) of BI 655064 (240 mg in total) on the same day for 3 weeks followed by one subcutaneous injection per week of 120 mg of BI 655064, up to 52 weeks.

Reporting group title	Placebo

Reporting group description:

Participants in the placebo group received two subcutaneous injections per week of placebo on the same day for 3 weeks followed by one subcutaneous injection per week of placebo, up to 52 weeks.

Serious adverse events	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 21 (28.57%)	6 / 20 (30.00%)	10 / 40 (25.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
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			

Foot fracture			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 40 (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			
Lymphocyte count decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 40 (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
Neutropenia			
subjects affected / exposed	1 / 21 (4.76%)	2 / 20 (10.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 2	1 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Eye disorders			
Chorioretinopathy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 40 (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
Ulcerative keratitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)

occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 40 (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
Dyspepsia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 40 (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
Oesophageal food impaction			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 40 (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
Liver injury			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus nephritis			

subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 40 (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
Proteinuria			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 40 (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			
Angioedema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 40 (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
Systemic lupus erythematosus			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis viral			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis infectious			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 40 (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			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 40 (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
Genital herpes simplex			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis cryptococcal			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Perineal abscess			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
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 bacterial			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary tuberculosis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	2 / 40 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 40 (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 / 21 (4.76%)	0 / 20 (0.00%)	0 / 40 (0.00%)

occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 40 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to	0 / 0		

treatment / all			
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Chorioretinopathy			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ulcerative keratitis			
subjects affected / exposed	0 / 40 (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 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspepsia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophageal food impaction			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cholelithiasis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver injury			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lupus nephritis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Proteinuria			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		

deaths causally related to treatment / all	0 / 0		
Systemic lupus erythematosus			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Conjunctivitis viral			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis infectious			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia bacteraemia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		

deaths causally related to treatment / all	0 / 0			
Genital herpes simplex				
subjects affected / exposed	0 / 40 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 40 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis cryptococcal				
subjects affected / exposed	0 / 40 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perineal abscess				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 40 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 40 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 40 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Pyelonephritis acute			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 40 (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 / 40 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	120 mg BI 655064	180 mg BI 655064	240 mg BI 655064
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 21 (80.95%)	13 / 20 (65.00%)	34 / 40 (85.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Hypotension			
subjects affected / exposed	0 / 21 (0.00%)	2 / 20 (10.00%)	1 / 40 (2.50%)
occurrences (all)	0	3	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 21 (9.52%)	1 / 20 (5.00%)	1 / 40 (2.50%)
occurrences (all)	2	1	3
Asthenia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 20 (0.00%)	1 / 40 (2.50%)

occurrences (all)	3	0	1
Injection site pain			
subjects affected / exposed	2 / 21 (9.52%)	1 / 20 (5.00%)	3 / 40 (7.50%)
occurrences (all)	2	1	3
Pyrexia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 20 (0.00%)	2 / 40 (5.00%)
occurrences (all)	4	0	2
Oedema peripheral			
subjects affected / exposed	3 / 21 (14.29%)	1 / 20 (5.00%)	3 / 40 (7.50%)
occurrences (all)	4	1	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 21 (4.76%)	2 / 20 (10.00%)	3 / 40 (7.50%)
occurrences (all)	1	3	4
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	6
Weight increased			
subjects affected / exposed	2 / 21 (9.52%)	2 / 20 (10.00%)	5 / 40 (12.50%)
occurrences (all)	2	2	8
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 20 (0.00%)	3 / 40 (7.50%)
occurrences (all)	3	0	6
Leukopenia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	4 / 40 (10.00%)
occurrences (all)	1	0	5
Lymphopenia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	5 / 40 (12.50%)
occurrences (all)	0	0	6
Neutropenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	6 / 40 (15.00%)
occurrences (all)	0	1	11
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Cough			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	5 / 40 (12.50%)
occurrences (all)	1	2	5
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 21 (4.76%)	2 / 20 (10.00%)	1 / 40 (2.50%)
occurrences (all)	1	2	1
Headache			
subjects affected / exposed	3 / 21 (14.29%)	1 / 20 (5.00%)	6 / 40 (15.00%)
occurrences (all)	3	1	8
Eye disorders			
Vision blurred			
subjects affected / exposed	2 / 21 (9.52%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	2	1	0
Dry eye			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 21 (23.81%)	3 / 20 (15.00%)	9 / 40 (22.50%)
occurrences (all)	6	4	9
Vomiting			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	2 / 40 (5.00%)
occurrences (all)	1	3	2
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	3 / 40 (7.50%)
occurrences (all)	1	0	4
Alopecia			
subjects affected / exposed	0 / 21 (0.00%)	3 / 20 (15.00%)	9 / 40 (22.50%)
occurrences (all)	0	3	9
Rash			
subjects affected / exposed	2 / 21 (9.52%)	0 / 20 (0.00%)	6 / 40 (15.00%)
occurrences (all)	2	0	9

Erythema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	4 / 40 (10.00%)
occurrences (all)	0	0	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 21 (14.29%)	0 / 20 (0.00%)	4 / 40 (10.00%)
occurrences (all)	3	0	5
Arthritis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	4 / 40 (10.00%)
occurrences (all)	0	1	4
Muscle spasms			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	1 / 40 (2.50%)
occurrences (all)	1	1	1
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 21 (4.76%)	3 / 20 (15.00%)	2 / 40 (5.00%)
occurrences (all)	1	3	2
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	2 / 21 (9.52%)	0 / 20 (0.00%)	1 / 40 (2.50%)
occurrences (all)	2	0	1
Hypokalaemia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	2 / 40 (5.00%)
occurrences (all)	0	1	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Gastroenteritis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	3 / 40 (7.50%)
occurrences (all)	0	1	3
Nasopharyngitis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 20 (5.00%)	4 / 40 (10.00%)
occurrences (all)	2	1	5
Herpes zoster			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	4 / 40 (10.00%)
occurrences (all)	0	1	4

Oral candidiasis			
subjects affected / exposed	2 / 21 (9.52%)	1 / 20 (5.00%)	0 / 40 (0.00%)
occurrences (all)	5	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	4
Rhinitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	4
Upper respiratory tract infection			
subjects affected / exposed	5 / 21 (23.81%)	6 / 20 (30.00%)	7 / 40 (17.50%)
occurrences (all)	6	9	8
Urinary tract infection			
subjects affected / exposed	1 / 21 (4.76%)	2 / 20 (10.00%)	4 / 40 (10.00%)
occurrences (all)	2	3	5

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 40 (87.50%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Hypotension			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Injection site pain			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		

Pyrexia subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2 2 / 40 (5.00%) 2		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1		
Investigations Lymphocyte count decreased subjects affected / exposed occurrences (all) Weight increased subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0 2 / 40 (5.00%) 3		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Lymphopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1 1 / 40 (2.50%) 3 1 / 40 (2.50%) 1 1 / 40 (2.50%) 1		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 3 1 / 40 (2.50%) 1		

Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 3 / 40 (7.50%) 3 5 / 40 (12.50%) 6		
Eye disorders Vision blurred subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all)	 0 / 40 (0.00%) 0 3 / 40 (7.50%) 3		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 6 / 40 (15.00%) 8 3 / 40 (7.50%) 4		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all)	 0 / 40 (0.00%) 0 7 / 40 (17.50%) 7 2 / 40 (5.00%) 2 3 / 40 (7.50%) 3		
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	7		
Arthritis			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Muscle spasms			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	0 / 40 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	10		
Herpes zoster			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Oral candidiasis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences (all)	1		

Respiratory tract infection subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 3		
Rhinitis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	8 / 40 (20.00%) 9		
Urinary tract infection subjects affected / exposed occurrences (all)	6 / 40 (15.00%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2015	Inclusion criterion 3 was revised to allow the inclusion of patients with a positive antidsDNA antibody at screening or around the time of start of induction therapy. Initially the patients had to have a positive anti-dsDNA antibody at screening. Exclusion criterion 9 ('live vaccination within 6 weeks before randomisation') was added.
02 February 2016	According to the updated SmPC for MMF, additional requirements for pregnancy tests and contraception methods, as well as recommendations regarding blood and semen donation were added in the respective sections of the CTP.
24 November 2016	Statements were included that vital status information was to be collected at Week 60 (EOS visit) for randomised patients who discontinued from the study before EOS. Inclusion criterion 1 was revised: Women of childbearing potential were to use '2 reliable methods of birth control, one of which should be highly effective' instead of '2 highly effective methods of birth control'. Also, in the definition of 'women of nonchildbearing potential', 'tubal occlusion' was removed as a sterilisation method. In exclusion criterion 4, the definition of antiphospholipid syndrome was modified. This had been requested by authorities. The following AEs were defined as AESIs (in addition to 'hepatic injury'): injection reactions including anaphylactic reaction, cytokine release syndrome, opportunistic infections and/or severe infections, lymphoproliferative disorders (e.g. B- and T-cell lymphoma, Non-Hodgkin lymphoma and Hodgkin lymphoma, hepatosplenic T-cell lymphoma), thrombosis and adjunct immunosuppression. Other additional changes have been applied.
17 February 2017	If a higher dose of i.v. steroids was considered necessary by the investigator, a total dose of up to 3 g was acceptable for initial induction treatment.
06 October 2017	Proteinuria at screening <3 g/day or ≥3 g/day was also defined as UP/UC <3 or UP/UC ≥3. Inclusion criterion 3 was modified: one of the documented criteria for SLE had to be a positive anti-dsDNA antibody or a positive antinuclear antibody. The following exclusion criterion was deleted: 'acute presence of oliguria (<500 mL/day)'. Further instructions with regard to steroids tapering were added.
07 September 2018	For the AESI 'opportunistic infections and/or severe infections', the following text was added as requested by the DMC: 'Whenever a patient comes to a visit and reports of an (S)AE related to infections, which occurred in the interval since the last visit, then he/she is routinely asked whether they have been seen/treated by a physician and whether blood samples had been taken in that context. Should this be answered in the affirmative, then efforts should be undertaken to collect the respective information'. A statement was added that if a partner of a male trial participant became pregnant this had to be reported and written consent of the pregnant partner was required.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported