



Clinical trial results:

An exploratory maintenance trial evaluating the effect of BI 655064 in Lupus Nephritis patients who have achieved a meaningful response either at the end of 1293.10 or after an induction treatment outside of 1293.10

Summary

EudraCT number	2017-003101-17
Trial protocol	CZ GR DE PT PL GB ES FR IT
Global end of trial date	27 July 2021

Results information

Result version number	v2 (current)
This version publication date	29 July 2022
First version publication date	28 May 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	1293-0013
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03385564
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, +1 18002430127, clintrriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim Call Center, Boehringer Ingelheim, +1 18002430127, clintrriage.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	09 November 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 May 2021
Global end of trial reached?	Yes
Global end of trial date	27 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this trial were to evaluate long-term efficacy and safety of different doses of BI 655064 versus placebo as add-on therapy to standard of care during maintenance treatment for lupus nephritis. The further objective of the trial was to study the effect of steroid tapering and steroid withdrawal during maintenance treatment.

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	22 January 2018
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: 1
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Hong Kong: 2
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	Malaysia: 1
Country: Number of subjects enrolled	Mexico: 13
Country: Number of subjects enrolled	Philippines: 4
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Thailand: 13
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 5
Worldwide total number of subjects	69
EEA total number of subjects	19

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)	69
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was to evaluate long-term efficacy and safety of different doses of BI 655064 versus placebo as add-on therapy to standard of care during maintenance treatment for lupus nephritis.

Pre-assignment

Screening details:

This is an extension trial with the requirement to entry that subjects responded to treatment in 1293.10 (NCT02770170) and had the desire to continue participation in a clinical trial. Subjects were screened for eligibility prior to participation in trial 1293.10 (NCT02770170).

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, Monitor, Carer, Data analyst, Assessor

Arms

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

Arm description:

120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Arm type	Experimental
Investigational medicinal product name	BI 655064 120 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Arm title	BI 655064 180 mg
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Arm description:

180 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Arm type	Experimental
Investigational medicinal product name	BI 655064 180 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

180 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Arm title	BI 655064 240 mg
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Arm description:

120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every week (240 mg every 2 weeks) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Arm type	Experimental
Investigational medicinal product name	BI 655064 240 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every week (240 mg every 2 weeks) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Arm title	Placebo
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Arm description:

Matching placebo were administered as solution for subcutaneous injection in a prefilled syringe once every week over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

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:

Matching placebo were administered as solution for subcutaneous injection in a prefilled syringe once every week over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Number of subjects in period 1	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg
Started	7	15	21
Intent to treat set	7	15	21
Completed	7	14	16
Not completed	0	1	5
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	-	-	3
Other than listed	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 1	Placebo
Started	26
Intent to treat set	26
Completed	17
Not completed	9
Adverse event, serious fatal	-
Consent withdrawn by subject	-
Adverse event, non-fatal	3
Other than listed	5
Lack of efficacy	1

Baseline characteristics

Reporting groups

Reporting group title	BI 655064 120 mg
Reporting group description:	
120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.	
Reporting group title	BI 655064 180 mg
Reporting group description:	
180 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.	
Reporting group title	BI 655064 240 mg
Reporting group description:	
120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every week (240 mg every 2 weeks) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.	
Reporting group title	Placebo
Reporting group description:	
Matching placebo were administered as solution for subcutaneous injection in a prefilled syringe once every week over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.	

Reporting group values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg
Number of subjects	7	15	21
Age categorical			
Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 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)	7	15	21
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 trial medication and were documented to have taken at least 1 dose of investigational treatment.			
Units: years			
arithmetic mean	31.9	36.5	35.4
standard deviation	± 6.5	± 8.7	± 10.5

Sex: Female, Male			
Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 dose of investigational treatment.			
Units: Participants			
Female	5	13	19
Male	2	2	2
Race (NIH/OMB)			
Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 dose of investigational treatment.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	6	9
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	3	9	11
More than one race	1	0	0
Unknown or Not Reported	1	0	0
Ethnicity (NIH/OMB)			
Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 dose of investigational treatment.			
Units: Subjects			
Hispanic or Latino	3	4	6
Not Hispanic or Latino	4	11	15
Unknown or Not Reported	0	0	0

Reporting group values	Placebo	Total	
Number of subjects	26	69	
Age categorical			
Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 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)	26	69	
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 trial medication and were documented to have taken at least 1 dose of investigational treatment.			
Units: years			
arithmetic mean	34.8		
standard deviation	± 10.9	-	

Sex: Female, Male			
Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 dose of investigational treatment.			
Units: Participants			
Female	24	61	
Male	2	8	
Race (NIH/OMB)			
Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 dose of investigational treatment.			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	11	28	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	1	
White	15	38	
More than one race	0	1	
Unknown or Not Reported	0	1	
Ethnicity (NIH/OMB)			
Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 dose of investigational treatment.			
Units: Subjects			
Hispanic or Latino	6	19	
Not Hispanic or Latino	20	50	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	BI 655064 120 mg
Reporting group description: 120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.	
Reporting group title	BI 655064 180 mg
Reporting group description: 180 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.	
Reporting group title	BI 655064 240 mg
Reporting group description: 120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every week (240 mg every 2 weeks) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.	
Reporting group title	Placebo
Reporting group description: Matching placebo were administered as solution for subcutaneous injection in a prefilled syringe once every week over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.	

Primary: Percentage of patients with complete renal response (CRR) and without any renal flares

End point title	Percentage of patients with complete renal response (CRR) and without any renal flares
End point description: The adjusted (model-based, adjusted for race and proteinuria at screening) percentage of patients with CRR and without any renal flares is reported. A logistic regression model was used including treatment and the covariates: race (Asian versus (vs.) non-Asian) and proteinuria <3 gram (g)/day vs. ≥3 g/day (or Urine protein (UP)/ Urine creatinine (UC) <3 vs. UP/UC ≥3) at screening. CRR was defined as urine protein (UP) < 0.5 g/day and either estimated glomerular filtration rate (eGFR) within normal range or decrease in eGFR < 20% from baseline 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 (TS) who had a baseline proteinuria (spot urine could be a used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.	
End point type	Primary
End point timeframe: At Week 52	

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	20	25
Units: Percentage of participants				
number (not applicable)	51.83	48.15	59.49	57.51

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	BI 655064 120 mg v Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7957
Method	Regression, Logistic
Parameter estimate	Difference
Point estimate	-5.68
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-34.192
upper limit	22.825

Statistical analysis title	Statistical Analysis 2
Comparison groups	BI 655064 180 mg v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5811
Method	Regression, Logistic
Parameter estimate	Difference
Point estimate	-9.37
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-31.178
upper limit	12.44

Statistical analysis title	Statistical Analysis 3
Comparison groups	BI 655064 240 mg v Placebo

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8972
Method	Regression, Logistic
Parameter estimate	Difference
Point estimate	1.97
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-17.534
upper limit	21.48

Secondary: Percentage of patients with confirmed complete renal response (CRR) and without any renal flares

End point title	Percentage of patients with confirmed complete renal response (CRR) and without any renal flares
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End point description:

The percentage of patients with confirmed complete renal response (CRR) (defined as CRR at both Week 42 and Week 52 using urine protein (UP)/urine creatine (UC) ratio [UP/UC] from the spot urines) and without any renal flares is reported. Complete renal response (CRR) was defined as urine protein (UP) < 0.5 g/day and either estimated glomerular filtration rate (eGFR) within normal range or decrease in eGFR < 20% from baseline 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 (TS) who had a baseline proteinuria (spot urine could be used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.

End point type	Secondary
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End point timeframe:

At Week 52

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	13	20	25
Units: Percentage of participants				
number (not applicable)	42.9	30.8	50.0	52.0

Statistical analyses

Statistical analysis title	Statistical Analysis 4
Comparison groups	BI 655064 120 mg v Placebo

Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.825
Method	Barnard test
Parameter estimate	Difference
Point estimate	-9.14
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-32.83
upper limit	17.02

Statistical analysis title	Statistical Analysis 6
Comparison groups	BI 655064 240 mg v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9632
Method	Barnard test
Parameter estimate	Difference
Point estimate	-2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-20.45
upper limit	16.62

Statistical analysis title	Statistical Analysis 5
Comparison groups	BI 655064 180 mg v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2562
Method	Barnard test
Parameter estimate	Difference
Point estimate	-21.23
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-39.44
upper limit	0.51

Secondary: Percentage of patients with proteinuria <0.8 grams (g)/day (d) and

without any renal flares at week 52

End point title	Percentage of patients with proteinuria <0.8 grams (g)/day (d) and without any renal flares at week 52
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End point description:

The percentage of patients with proteinuria <0.8 grams (g)/day (d) and without any renal flares at week 52 is reported.

Intent to treat (ITT) set: this patient set included all patients from the treated set (TS) who had a baseline proteinuria (spot urine could be used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.

End point type	Secondary
End point timeframe:	
At Week 52	

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	20	25
Units: Percentage of participants				
number (not applicable)	57.1	50.0	60.0	60.0

Statistical analyses

Statistical analysis title	Statistical Analysis 7
Comparison groups	BI 655064 120 mg v Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9275
Method	Barnard test
Parameter estimate	Difference
Point estimate	-2.86
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-28.58
upper limit	21.1

Statistical analysis title	Statistical Analysis 9
Comparison groups	BI 655064 240 mg v Placebo

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference
Point estimate	0
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-18.37
upper limit	18.07

Statistical analysis title	Statistical Analysis 8
Comparison groups	BI 655064 180 mg v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6064
Method	Barnard test
Parameter estimate	Difference
Point estimate	-10
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-29.9
upper limit	10.64

Secondary: Percentage of patients with complete renal response (CRR) at week 52 and sustained steroid reduction to ≤ 5 milligrams (mg)/day (d) from Week 26 to Week 52

End point title	Percentage of patients with complete renal response (CRR) at week 52 and sustained steroid reduction to ≤ 5 milligrams (mg)/day (d) from Week 26 to Week 52
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End point description:

The percentage of patients with complete renal response (CRR) at Week 52 and sustained steroid reduction to ≤ 5 milligrams (mg)/day (d) from Week 26 to Week 52 is reported. Complete renal response (CRR) was defined as urine protein (UP) < 0.5 g/day and either estimated glomerular filtration rate (eGFR) within normal range or decrease in eGFR $< 20\%$ from baseline 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 (TS) who had a baseline proteinuria (spot urine could be used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.

End point type	Secondary
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End point timeframe:

At Week 52 (Sustained Steroid Reduction to ≤ 5 mg/d was evaluated from Week 26 to Week 52).

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	18	23
Units: Percentage of participants				
number (not applicable)	42.9	42.9	55.6	39.1

Statistical analyses

Statistical analysis title	Statistical Analysis 10
Comparison groups	BI 655064 120 mg v Placebo
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9119
Method	Barnard test
Parameter estimate	Difference
Point estimate	3.73
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-20.53
upper limit	29.6

Statistical analysis title	Statistical Analysis 11
Comparison groups	BI 655064 180 mg v Placebo
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.851
Method	Barnard test
Parameter estimate	Difference
Point estimate	3.73
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-16.58
upper limit	24.31

Statistical analysis title	Statistical Analysis 12
Comparison groups	BI 655064 240 mg v Placebo

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3498
Method	Barnard test
Parameter estimate	Difference
Point estimate	16.43
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-3.53
upper limit	34.73

Secondary: Percentage of patients experiencing at least one renal flare during 52 weeks

End point title	Percentage of patients experiencing at least one renal flare during 52 weeks
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End point description:

The percentage of patients experiencing at least one renal flare during 52 weeks is reported.

Intent to treat (ITT) set: this patient set included all patients from the treated set (TS) who had a baseline proteinuria (spot urine could be used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.

End point type	Secondary
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End point timeframe:

At Week 52

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	21	25
Units: Percentage of participants				
number (not applicable)	0	21.4	0	16.0

Statistical analyses

Statistical analysis title	Statistical Analysis 13
Comparison groups	BI 655064 180 mg v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7921
Method	Barnard test
Parameter estimate	Difference
Point estimate	5.43

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-10.19
upper limit	23.57

Secondary: Time to first renal flare over the course of 52 weeks

End point title	Time to first renal flare over the course of 52 weeks
End point description:	
The time to first renal flare over the course of 52 weeks is reported.	
Intent to treat (ITT) set: this patient set included all patients from the treated set (TS) who had a baseline proteinuria (spot urine could be a used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subject with non-missing results were included in the analysis.	
End point type	Secondary
End point timeframe:	
Up to 52 weeks.	

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[1]	3	0 ^[2]	4
Units: Weeks				
median (full range (min-max))	(to)	36.0 (26 to 52)	(to)	37.5 (6 to 52)

Notes:

[1] - Only subject with non-missing results were included in the analysis.

[2] - Only subject with non-missing results were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with partial renal response (PRR) and without any renal flares derived from urine protein (UP) 24 hours (h) collection at Week 52

End point title	Percentage of patients with partial renal response (PRR) and without any renal flares derived from urine protein (UP) 24 hours (h) collection at Week 52
End point description:	
The percentage of patients with partial renal response (PRR) and without any renal flares derived from urine protein (UP) 24 hours (h) collection at Week 52 is reported. 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 (TS) who had a baseline proteinuria (spot urine could be a used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.	
End point type	Secondary

End point timeframe:

At Week 52

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	20	25
Units: Percentage of participants				
number (not applicable)	100.0	64.3	75.0	68.0

Statistical analyses

Statistical analysis title	Statistical Analysis 14
Comparison groups	BI 655064 120 mg v Placebo
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1016
Method	Barnard test
Parameter estimate	Difference
Point estimate	32
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	10.28
upper limit	44.74

Statistical analysis title	Statistical Analysis 16
Comparison groups	BI 655064 240 mg v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6247
Method	Barnard test
Parameter estimate	Difference
Point estimate	7
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-10.5
upper limit	23.31

Statistical analysis title	Statistical Analysis 15
Comparison groups	BI 655064 180 mg v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8323
Method	Barnard test
Parameter estimate	Difference
Point estimate	-3.71
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-23.79
upper limit	15.29

Secondary: Change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) total score at Week 12

End point title	Change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) total score at Week 12
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End point description:

Change from baseline in SLEDAI total score at Week 12 is calculated as: value at Week 12 - value at baseline. SLEDAI assessment consists of 24 items capturing non-renal and renal symptoms. The total score captures non-renal and renal symptoms. Each of the 24 items has a score ranging from 1 to 8. A participant will get the score if the event of the item presents, while 0 if not. 8 items have the score 8, 6 items have the score 4, 7 items have the score 2, and 3 items have the score 1. The SLEDAI Total score is the sum of the scores of the 24 items, ranging from 0 (better health) to 105 (worse health).

Intent to treat (ITT) set: this patient set included all patients from the treated set (TS) who had a baseline proteinuria (spot urine could be used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.

End point type	Secondary
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End point timeframe:

At baseline and at Week 12

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	13	18	25
Units: Score on a scale				
arithmetic mean (standard deviation)	-8.4 (± 5.8)	-7.5 (± 4.3)	-9.3 (± 4.9)	-7.7 (± 6.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Systemic Lupus Erythematosus Disease Activity

Index (SLEDAI) total score at Week 26

End point title	Change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) total score at Week 26
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End point description:

Change from baseline in SLEDAI total score at Week 26 is calculated as: value at Week 26 - value at baseline. SLEDAI assessment consists of 24 items capturing non-renal and renal symptoms. The total score captures non-renal and renal symptoms. Each of the 24 items has a score ranging from 1 to 8. A participant will get the score if the event of the item presents, while 0 if not. 8 items have the score 8, 6 items have the score 4, 7 items have the score 2, and 3 items have the score 1. The SLEDAI Total score is the sum of the scores of the 24 items, ranging from 0 (better health) to 105 (worse health).

Intent to treat (ITT) set: this patient set included all patients from the treated set (TS) who had a baseline proteinuria (spot urine could be used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.

End point type	Secondary
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End point timeframe:

At baseline and at Week 26

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	16	21
Units: Score on a scale				
arithmetic mean (standard deviation)	-8.7 (± 5.7)	-7.9 (± 3.5)	-11.3 (± 4.8)	-5.9 (± 5.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) total score at Week 42

End point title	Change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) total score at Week 42
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End point description:

Change from baseline in SLEDAI total score at Week 42 is calculated as: value at Week 42 - value at baseline. SLEDAI assessment consists of 24 items capturing non-renal and renal symptoms. The total score captures non-renal and renal symptoms. Each of the 24 items has a score ranging from 1 to 8. A participant will get the score if the event of the item presents, while 0 if not. 8 items have the score 8, 6 items have the score 4, 7 items have the score 2, and 3 items have the score 1. The SLEDAI Total score is the sum of the scores of the 24 items, ranging from 0 (better health) to 105 (worse health).

Intent to treat (ITT) set: this patient set included all patients from the treated set (TS) who had a baseline proteinuria (spot urine could be used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.

End point type	Secondary
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End point timeframe:

At baseline and at Week 42

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	9	13
Units: Score on a scale				
arithmetic mean (standard deviation)	-6.6 (± 3.4)	-6.3 (± 2.4)	-11.1 (± 5.1)	-6.5 (± 6.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) total score at Week 52

End point title	Change from baseline in Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) total score at Week 52
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End point description:

Change from baseline in SLEDAI total score at Week 52 is calculated as: value at Week 52 - value at baseline. SLEDAI assessment consists of 24 items capturing non-renal and renal symptoms. The total score captures non-renal and renal symptoms. Each of the 24 items has a score ranging from 1 to 8. A participant will get the score if the event of the item presents, while 0 if not. 8 items have the score 8, 6 items have the score 4, 7 items have the score 2, and 3 items have the score 1. The SLEDAI Total score is the sum of the scores of the 24 items, ranging from 0 (better health) to 105 (worse health).

Intent to treat (ITT) set: this patient set included all patients from the treated set (TS) who had a baseline proteinuria (spot urine could be used if the patient did not have 24 hours urine collections) and a baseline Estimated glomerular filtration rate (eGFR) value. Only subjects with non-missing results were included in the analysis.

End point type	Secondary
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End point timeframe:

At baseline and at Week 52

End point values	BI 655064 120 mg	BI 655064 180 mg	BI 655064 240 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	16	17
Units: Score on a scale				
arithmetic mean (standard deviation)	-8.9 (± 6.1)	-7.2 (± 4.0)	-10.6 (± 4.9)	-5.3 (± 8.0)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For serious and non-serious adverse events: From first dose of trial medication until last dose + 50 days of residual effect period, up to 52 weeks + 50 days. For all-cause mortality: From first dose of trial medication until end of study, up to 64 weeks.

Adverse event reporting additional description:

Treated set (TS): this patient set included all patients who were dispensed trial medication and were documented to have taken at least 1 dose of investigational treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	BI 655064 120 mg
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Reporting group description:

120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Reporting group title	Placebo
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Reporting group description:

Matching placebo were administered as solution for subcutaneous injection in a prefilled syringe once every week over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Reporting group title	BI 655064 240 mg
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Reporting group description:

120 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every week (240 mg every 2 weeks) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Reporting group title	BI 655064 180 mg
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Reporting group description:

180 milligrams (mg) BI 655064 were administered as solution for subcutaneous injection in a prefilled syringe once every 2 weeks plus the administration of matching placebo as subcutaneous injection in a prefilled syringe once every 2 weeks (in the alternative weeks without BI 655064 administration) over a treatment period of 52 weeks, followed by a 12-week follow-up period. The patients received 1 injection per week.

Serious adverse events	BI 655064 120 mg	Placebo	BI 655064 240 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	4 / 26 (15.38%)	6 / 21 (28.57%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ocular lymphoma			

subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	8 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 21 (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
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 21 (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
Pulmonary hypertension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 21 (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
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (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
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 21 (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
Nervous system disorders			

Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Haemobilia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 21 (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
Skin and subcutaneous tissue disorders			
Panniculitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			

subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
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			
Crystal arthropathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 21 (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			
Clostridium difficile infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis enterococcal			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nocardiosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pelvic abscess			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis of central nervous system			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BI 655064 180 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ocular lymphoma			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal			

disorders			
Pneumothorax			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Haemobilia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Panniculitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Crystal arthropathy			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myalgia			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Systemic lupus erythematosus			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Clostridium difficile infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis enterococcal			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nocardiosis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pelvic abscess			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tuberculosis of central nervous system			
subjects affected / exposed	0 / 15 (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	BI 655064 120 mg	Placebo	BI 655064 240 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	15 / 26 (57.69%)	15 / 21 (71.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Chills			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Oedema			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Menometrorrhagia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Adenomyosis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 26 (7.69%) 2	0 / 21 (0.00%) 0
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 26 (3.85%) 1	2 / 21 (9.52%) 2
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 26 (3.85%) 1	0 / 21 (0.00%) 0
Blood lactate dehydrogenase decreased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Urine protein/creatinine ratio increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 26 (3.85%) 1	0 / 21 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 26 (7.69%) 2	0 / 21 (0.00%) 0
Injury, poisoning and procedural complications			

Chillblains subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Ligament sprain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 26 (3.85%) 1	0 / 21 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 26 (3.85%) 3	1 / 21 (4.76%) 1
Syncope subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	2 / 26 (7.69%) 2	0 / 21 (0.00%) 0
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 26 (3.85%) 1	0 / 21 (0.00%) 0
Eye disorders Cataract subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Photopsia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Visual field defect subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Gastrointestinal disorders Abdominal pain			

subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	2 / 26 (7.69%)	1 / 21 (4.76%)
occurrences (all)	1	2	1
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	1 / 21 (4.76%)
occurrences (all)	0	3	1
Butterfly rash			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 21 (4.76%)
occurrences (all)	0	2	1
Onychoclasia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	4 / 21 (19.05%)
occurrences (all)	0	3	5
Subacute cutaneous lupus erythematosus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Urticaria			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 26 (0.00%) 0	0 / 21 (0.00%) 0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	0 / 21 (0.00%)
occurrences (all)	0	6	0
Lupus nephritis			
subjects affected / exposed	0 / 7 (0.00%)	2 / 26 (7.69%)	0 / 21 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	2 / 21 (9.52%)
occurrences (all)	0	1	2
Arthritis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	0 / 21 (0.00%)
occurrences (all)	0	1	0
Oligoarthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Coronavirus infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Herpes zoster			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Periodontitis			

subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	1 / 21 (4.76%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 26 (3.85%)	0 / 21 (0.00%)
occurrences (all)	1	1	0
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	3 / 26 (11.54%)	5 / 21 (23.81%)
occurrences (all)	1	3	6
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	3 / 26 (11.54%)	3 / 21 (14.29%)
occurrences (all)	0	3	4
Vaginal infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	1	0	0
Glucose tolerance impaired			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 26 (3.85%)	1 / 21 (4.76%)
occurrences (all)	0	2	2
Iron deficiency			
subjects affected / exposed	0 / 7 (0.00%)	0 / 26 (0.00%)	0 / 21 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BI 655064 180 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 15 (73.33%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Hypotension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Menometrorrhagia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Adenomyosis			

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all) Upper-airway cough syndrome subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0 0 / 15 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) Blood lactate dehydrogenase decreased subjects affected / exposed occurrences (all) Urine protein/creatinine ratio increased subjects affected / exposed occurrences (all) Weight increased subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 2 / 15 (13.33%) 2 0 / 15 (0.00%) 0		
Injury, poisoning and procedural complications Chillblains subjects affected / exposed occurrences (all) Ligament sprain	1 / 15 (6.67%) 1		

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		
Nervous system disorders			
Headache			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Syncope			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Vertigo			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Eye disorders			
Cataract			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Photopsia			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Visual field defect			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Abdominal pain upper			
subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		

Diarrhoea			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	4		
Dyspepsia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Butterfly rash			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Onychoclasia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Subacute cutaneous lupus erythematosus			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Lupus nephritis			

subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Arthritis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Oligoarthritis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Coronavirus infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Herpes simplex			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Periodontitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Respiratory tract infection			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Vaginal infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Dyslipidaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Glucose tolerance impaired			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Iron deficiency			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 May 2018	<ul style="list-style-type: none">- Plasma concentrations of BI 655064 and anti-BI 655064 antibody response were added as further endpoints to align with the objectives of the trial- In inclusion criterion 1, contraception instructions for patients on AZA were added following inclusion of Azathioprine (AZA) as background medication allowed in any case in the trial- A statement was included that Mycophenolate mofetil (MMF) and AZA were considered auxiliary medicinal products in the trial- A statement was added that the patients who did not follow glucocorticoid tapering scheme due to medical reasons would not be excluded from the trial- AZA was allowed as background medication in any case- The version of SLEDAI-2K assessment was corrected to SELENA-SLEDAI to align with the predecessor trial (1293-0010) in which SELENA-SLEDAI was used- A statement was added that genotyping of patients rolling over from trial 1293-0010 was already performed and was not to be repeated- The time window between End of treatment (EOT) of trial 1293-0010 and Visit 1 of trial 1293-0013 was reduced from 7 to 3 days to avoid treatment interruption- The time window for follow-up visits for early discontinued patients was changed from 8 to 12 weeks to align with the follow-up period of 12 weeks for patients who completed the treatment.

21 December 2020	<ul style="list-style-type: none"> - The start of Group 2 (constituting patients recruited outside of trial 1293-0010) was cancelled based on the outcome of trial 1293-0010, and all references to Group 2 were removed from the CTP accordingly - Immunology tests (C3/C4 complement, anti-dsDNA) were added to Visit 8 (Week 42) to be consistent with the requirements of the SLEDAI questionnaire - New safety and efficacy data from the final analysis of 1293-0010 were included to better describe drug profile - An infection risk-assessment and stopping rules in the COVID-19 pandemic were added to account for the COVID-19 pandemic situation - Baseline values were redefined in Section 2.1.1 'Main Objectives' to enable analysis of outcomes in the full 2-year treatment period in trials 1293-0010 and 1293-0013 - A primary endpoint from 1293-0010 ('Proportion of patients with CRR at Week 52') and 'Proportion of patients with confirmed CRR' endpoint from 1293-0010 were added as secondary endpoints. However, the former was not analysed according to changes introduced by the TSAP - The following further endpoints were added: 'Proportion of patients with CRR and without any renal flares at Week 26' (to allow comparison of outcomes after the 1.5-year treatment period to competitor trials), 'Proportion of patients with CRR based on spot urine and without any renal flares at Week 52' (based on learnings from the final analysis of trial 1293-0010), 'Average daily steroid dose in 1293-0013 and average daily steroid dose from Week 13 of trial 1293-0010 to end of treatment in 1293-0013' (to allow comparison of daily steroid dose over the whole treatment period), 'Change from baseline in each renal, non-renal and clinical part of the SLEDAI at Weeks 12, 26, 42, and 52', 'Change from baseline in SLEDAI domains at Weeks 12, 26, 42, and 52' (to allow a more detailed analysis of changes in the SLEDAI).
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported