



## 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 |
|-----------------------|-----------|

#### 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:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| 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              |
| <b>Arm title</b>             | 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.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | BI 655064 180 mg |
|------------------|------------------|

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.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | BI 655064 240 mg |
|------------------|------------------|

**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.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

**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.

| <b>Number of subjects in period 1</b> | 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                      | -                | -                | -                |

| <b>Number of subjects in period 1</b> | 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:<br>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:<br>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:<br>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:<br>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:<br>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.<br>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.<br><br>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:<br>At Week 52                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                        |

| <b>End point values</b>           | 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

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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                     |

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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                      |

|                                   |                            |
|-----------------------------------|----------------------------|
| <b>Statistical analysis title</b> | 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 |
|-----------------|--------------------------------------------------------------------------------------------------|

### 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 |
|----------------|-----------|

### 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         |

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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                      |

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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 |
|-----------------|--------------------------------------------------------------------------------------------------------|

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**

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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                       |

|                                   |                            |
|-----------------------------------|----------------------------|
| <b>Statistical analysis title</b> | 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         |

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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 $\leq 5$ 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 $\leq 5$ milligrams (mg)/day (d) from Week 26 to Week 52 |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|

#### **End point description:**

The percentage of patients with complete renal response (CRR) at Week 52 and sustained steroid reduction to  $\leq 5$  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 |
|----------------|-----------|

#### **End point timeframe:**

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

| <b>End point values</b>           | 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

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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                       |

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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                      |

|                                   |                            |
|-----------------------------------|----------------------------|
| <b>Statistical analysis title</b> | 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 |
|-----------------|------------------------------------------------------------------------------|

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 |
|----------------|-----------|

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

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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 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 <sup>[1]</sup> | 3                | 0 <sup>[2]</sup> | 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 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                      |

|                                         |                            |
|-----------------------------------------|----------------------------|
| <b>Statistical analysis title</b>       | 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 |
|-----------------|-------------------------------------------------------------------------------------------------------------|

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 |
|----------------|-----------|

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 |
|-----------------|-------------------------------------------------------------------------------------------------------------|

### 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 |
|----------------|-----------|

### 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 |
|-----------------|-------------------------------------------------------------------------------------------------------------|

### 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 |
|----------------|-----------|

### 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 |
|-----------------|-------------------------------------------------------------------------------------------------------------|

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 |
|----------------|-----------|

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 |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### 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 | 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 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 | 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.

| 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          |

|                                                                     |                  |  |  |
|---------------------------------------------------------------------|------------------|--|--|
| <b>Serious adverse events</b>                                       | 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 %

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

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

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

|                                                  |                     |  |  |
|--------------------------------------------------|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>1 |  |  |
| Nervous system disorders                         |                     |  |  |
| Headache                                         |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Syncope                                          |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Blood and lymphatic system disorders             |                     |  |  |
| Neutropenia                                      |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Ear and labyrinth disorders                      |                     |  |  |
| Ear pain                                         |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Vertigo                                          |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Eye disorders                                    |                     |  |  |
| Cataract                                         |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Photopsia                                        |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Visual field defect                              |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Gastrointestinal disorders                       |                     |  |  |
| Abdominal pain                                   |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 |  |  |
| Abdominal pain upper                             |                     |  |  |
| subjects affected / exposed<br>occurrences (all) | 1 / 15 (6.67%)<br>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<br>occurrences (all) | 0 / 15 (0.00%)<br>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"><li>- Plasma concentrations of BI 655064 and anti-BI 655064 antibody response were added as further endpoints to align with the objectives of the trial</li><li>- 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</li><li>- A statement was included that Mycophenolate mofetil (MMF) and AZA were considered auxiliary medicinal products in the trial</li><li>- 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</li><li>- AZA was allowed as background medication in any case</li><li>- 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</li><li>- A statement was added that genotyping of patients rolling over from trial 1293-0010 was already performed and was not to be repeated</li><li>- 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</li><li>- 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.</li></ul> |

|                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 21 December 2020 | <ul style="list-style-type: none"> <li>- 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</li> <li>- Immunology tests (C3/C4 complement, anti-dsDNA) were added to Visit 8 (Week 42) to be consistent with the requirements of the SLEDAI questionnaire</li> <li>- New safety and efficacy data from the final analysis of 1293-0010 were included to better describe drug profile</li> <li>- An infection risk-assessment and stopping rules in the COVID-19 pandemic were added to account for the COVID-19 pandemic situation</li> <li>- 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</li> <li>- 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</li> <li>- 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).</li> </ul> |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported