# Clinical trial results:
# A Prospective, Double-blind, Randomized, Placebo-controlled, Repeated dose, Multicentre Phase IIa Proof-of-Concept Study with BT063 in Subjects with Systemic Lupus Erythematosus (BT063 in SLE)

## Summary

| | |
|---|---|
| EudraCT number | 2014-005526-35 |
| Trial protocol | PL |
| Global end of trial date | 25 October 2017 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 13 December 2021 |
| First version publication date | 13 December 2021 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | 990 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02554019 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Biotest AG |
| Sponsor organisation address | Landsteinerstr. 5, Dreieich, Germany, 63303 |
| Public contact | Director Operations & Systems, Corporate Clinical Research & Development, Biotest AG, 49 61038010, peter.roettgen@biotest.com |
| Scientific contact | Director Operations & Systems, Corporate Clinical Research & Development, Biotest AG, 49 61038010, peter.roettgen@biotest.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 | 25 October 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 October 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 October 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

This study has 2 parts.
The primary objective of Part I of this study is to evaluate the safety and tolerability of 3 months of treatment with 50 mg BT063 versus placebo in subjects with SLE.
The primary objective of Part II of this study is to evaluate the safety and tolerability of either 25 mg, 50, mg or 100 mg BT063 versus placebo in subjects with SLE. The dose level for Part II will be determined based on an interim analysis conducted after the last subject of Part I has completed the treatment.

Protection of trial subjects:

After the end of the first 2-hour infusion of IMP (D0 [baseline]), the subject must stay at the investigational site for at least an additional 2 hours to enable monitoring for a type I hypersensitivity reaction. At all subsequent visits the subject should be observed for at least half an hour after the infusion of IMP.

Adverse Events of Special Interest
Adverse Events of special interest (AESI; serious or nonserious) are events that are of scientific and medical concern specific to the Sponsor's product for which close monitoring and rapid communication by the investigator to the Sponsor is appropriate. For this study, the following AEs of special interest will be recorded:

- Aphthous mouth ulcers (new, recurrent or aggravation of pre-existing lesions)
- Any other GI ulcers or significant GI symptoms (e.g., pain, blood in stool, dyspepsia or similar)

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 28 September 2015 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 3 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Belarus: 9 |
| Country: Number of subjects enrolled | Georgia: 6 |
| Country: Number of subjects enrolled | Serbia: 7 |
| Country: Number of subjects enrolled | Poland: 14 |
| Worldwide total number of subjects | 36 |
| EEA total number of subjects | 14 |

Notes:

| Subjects enrolled per age group | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 33 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment period: 01 Sep 2015 to 05 Apr 2017.
A total of 12 study sites enrolled subjects into the study in 4 countries: Georgia, Poland, Belarus, and Serbia.

### Pre-assignment

Screening details:

Adult subjects had SLE as defined by ACR criteria such that ≥ 4 of the 11 criteria were met for ≥ 3 months before screening,
moderate to severe SLE disease activity at screening and baseline demonstrated by SLEDAI-2K total score ≥ 6, including skin and joint involvement (CLASI ≥ 5 or at least 5 of 66/68 joints with pain and signs of inflammation)

### Period 1

| | |
|---|---|
| Period 1 title | overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Blinding implementation details:

Subjects, investigators, and study personnel will remain blinded with regard to the randomized treatment assignment until after database lock.
An interactive web response system (IWRS) will be implemented and used for randomization and IMP re supply.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | BT063 Placebo |

Arm description:

End formulation buffer without BT063 drug product

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | BT063 Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

The IMP was available in single-use vials containing 1.0 mL placebo. During Part I of the study, 1.0 mL IMP was diluted in 20 mL of a physiological sodium chloride solution (0.9% NaCl solution). During Part II 2.0 mL IMP was used. The diluted IMP was infused completely via a perfusor pump at an infusion rate of 10 mL/h.

| | |
|---|---|
| **Arm title** | BT063 50mg |

Arm description:

BT063 provided as a sterile solution containing the IL-10 binding monoclonal antibody (mAb)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | BT063 50 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BT063 50mg: The IMP was available in single-use vials containing 1.0 mL BT063 (50mg/ml). During Part

I of the study, 1.0 mL IMP was diluted in 20 mL of a physiological sodium chloride solution (0.9% NaCl solution). The diluted IMP was infused completely via a perfusor pump at an infusion rate of 10 mL/h.

| **Arm title** | BT063 100mg |
|---|---|
| Arm description: | |
| BT063 will be provided as a sterile solution containing the IL-10 binding monoclonal antibody (mAb) | |
| Arm type | Experimental |
| Investigational medicinal product name | BT063 100mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BT063 100mg: The IMP was available in single-use vials containing 1.0 mL BT063 (50mg/ml). During Part II of the study, 2.0 mL IMP was diluted in 20 mL of a physiological sodium chloride solution (0.9% NaCl solution). The diluted IMP was infused completely via a perfusor pump at an infusion rate of 10 mL/h.

| **Number of subjects in period 1** | BT063 Placebo | BT063 50mg | BT063 100mg |
|---|---|---|---|
| Started | 12 | 12 | 12 |
| Completed | 10 | 10 | 12 |
| Not completed | 2 | 2 | 0 |
| Consent withdrawn by subject | 2 | 1 | - |
| Adverse event, non-fatal | - | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | BT063 Placebo |
| Reporting group description: | |
| End formulation buffer without BT063 drug product | |
| Reporting group title | BT063 50mg |
| Reporting group description: | |
| BT063 provided as a sterile solution containing the IL-10 binding monoclonal antibody (mAb) | |
| Reporting group title | BT063 100mg |
| Reporting group description: | |
| BT063 will be provided as a sterile solution containing the IL-10 binding monoclonal antibody (mAb) | |

| Reporting group values | BT063 Placebo | BT063 50mg | BT063 100mg |
|---|---|---|---|
| Number of subjects | 12 | 12 | 12 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous | | | |
| age of 18-75 years (inclusive) | | | |
| Units: years<br>median<br>full range (min-max) | <br>43.5<br>30 to 68 | <br>35.5<br>21 to 61 | <br>53.0<br>38 to 59 |
| Gender categorical | | | |
| Male or Female | | | |
| Units: Subjects | | | |
| Female<br>Male | 12<br>0 | 10<br>2 | 11<br>1 |
| Have a family history of lupus | | | |
| subject number and proportion, who had a family history of lupus, were collected | | | |
| Units: Subjects | | | |
| Yes<br>No<br>Unknown | 1<br>10<br>1 | 0<br>11<br>1 | 0<br>11<br>1 |
| Race<br>Units: Subjects | | | |
| white | 12 | 12 | 12 |

| Reporting group values | Total | | |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Number of subjects | 36 | | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| age of 18-75 years (inclusive) | | | |
| Units: years | | | |
| median | | | |
| full range (min-max) | - | | |
| Gender categorical | | | |
| Male or Female | | | |
| Units: Subjects | | | |
| Female | 33 | | |
| Male | 3 | | |
| Have a family history of lupus | | | |
| subject number and proportion, who had a family history of lupus, were collected | | | |
| Units: Subjects | | | |
| Yes | 1 | | |
| No | 32 | | |
| Unknown | 3 | | |
| Race<br>Units: Subjects | | | |
| white | 36 | | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Safety Set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The safety set comprises all subjects who have received the study medication at least once.

| | |
|---|---|
| Subject analysis set title | Intention-to-treat set: |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The intention-to treat (ITT) set consists of all subjects who have received any study medication and have at least 1 post-baseline efficacy measurement.

| **Reporting group values** | Safety Set | Intention-to-treat set: | |
|---|---|---|---|
| Number of subjects | 36 | 36 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | | | |

| | | | |
|---|---|---|---|
| Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous | | | |
| age of 18-75 years (inclusive) | | | |
| Units: years | | | |
| median | 44.5 | 44.5 | |
| full range (min-max) | 21 to 68 | 21 to 68 | |
| Gender categorical | | | |
| Male or Female | | | |
| Units: Subjects | | | |
| Female | 33 | 33 | |
| Male | 3 | 3 | |
| Have a family history of lupus | | | |
| subject number and proportion, who had a family history of lupus, were collected | | | |
| Units: Subjects | | | |
| Yes | 1 | 1 | |
| No | 32 | 32 | |
| Unknown | 3 | 3 | |
| Race<br>Units: Subjects | | | |
| white | 36 | 36 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | BT063 Placebo |
| Reporting group description: | |
| End formulation buffer without BT063 drug product | |
| Reporting group title | BT063 50mg |
| Reporting group description: | |
| BT063 provided as a sterile solution containing the IL-10 binding monoclonal antibody (mAb) | |
| Reporting group title | BT063 100mg |
| Reporting group description: | |
| BT063 will be provided as a sterile solution containing the IL-10 binding monoclonal antibody (mAb) | |
| Subject analysis set title | Safety Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The safety set comprises all subjects who have received the study medication at least once. | |
| Subject analysis set title | Intention-to-treat set: |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| The intention-to treat (ITT) set consists of all subjects who have received any study medication and have at least 1 post-baseline efficacy measurement. | |

### Primary: Incidence of AEs

| | |
|---|---|
| End point title | Incidence of AEs[1] |
| End point description: | |
| Incidence of AEs (including SAEs and AEs leading to discontinuation) from baseline (week 0) to week 14 | |
| End point type | Primary |
| End point timeframe: | |
| From baseline (week 0) to week 14 | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Explorative descriptive statistics were used for all variables. No statistical tests were performed.

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | Safety Set |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 12 | 12 | 12 | 36 |
| Units: events | 14 | 12 | 32 | 58 |

### Statistical analyses

No statistical analyses for this end point

### Primary: Changes in safety parameters

| | |
|---|---|
| End point title | Changes in safety parameters[2] |
| End point description: | |

Changes from baseline in the following safety parameters were assessed:
- Physical examinations

- Vital signs
- ECGs
- Safety laboratory parameters (full blood count including white differential count, clinical chemistry, thyroid hormones, urinalysis, and faecal occult blood test)
- Development of anti-drug antibodies against BT063 (anti-BT063)
- Immunological status of potential viral and bacterial infections (HBV, HCV, HIV, tetanus, diphtheria tuberculosis)
- EBV / CMV Serology
- Premature withdrawals

| End point type | Primary |
|---|---|

End point timeframe:

From baseline (week 0) to week 14

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Explorative descriptive statistics were used for all variables. No statistical tests were performed.

| **End point values** | BT063 Placebo | BT063 50mg | BT063 100mg | Safety Set |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 12 | 12 | 12 | 36 |
| Units: subject with any safety relevant change | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Subject with TEAEs

| End point title | Subject with TEAEs[3] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

From baseline (week 0) to week 14

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Explorative descriptive statistics were used for all variables. No statistical tests were performed.

| **End point values** | BT063 Placebo | BT063 50mg | BT063 100mg | Safety Set |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 12 | 12 | 12 | 36 |
| Units: subjects | 8 | 5 | 8 | 21 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Subjects with TEAEs leading to early termination

| End point title | Subjects with TEAEs leading to early termination[4] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

From baseline (week 0) to week 14

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Explorative descriptive statistics were used for all variables. No statistical tests were performed.

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | Safety Set |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 12 | 12 | 12 | 36 |
| Units: subjects | 0 | 1 | 0 | 1 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Subjects with treatment-emergent SAEs

| End point title | Subjects with treatment-emergent SAEs[5] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

From baseline (week 0) to week 14

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Explorative descriptive statistics were used for all variables. No statistical tests were performed.

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | Safety Set |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 12 | 12 | 12 | 36 |
| Units: subjects | 0 | 1 | 1 | 2 |

### Statistical analyses

No statistical analyses for this end point

## Primary: Subjects with drug-related TEAEs

| End point title | Subjects with drug-related TEAEs[6] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

From baseline (week 0) to week 14

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Explorative descriptive statistics were used for all variables. No statistical tests were performed.

| **End point values** | BT063 Placebo | BT063 50mg | BT063 100mg | Safety Set |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 12 | 12 | 12 | 36 |
| Units: subjects | 0 | 1 | 2 | 3 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Subjects with severe TEAEs

| End point title | Subjects with severe TEAEs[7] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

From baseline (week 0) to week 28

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Explorative descriptive statistics were used for all variables. No statistical tests were performed.

| **End point values** | BT063 Placebo | BT063 50mg | BT063 100mg | Safety Set |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 12 | 12 | 12 | 36 |
| Units: subjects | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Subjects with TEAEs leading to death

| End point title | Subjects with TEAEs leading to death[8] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

From baseline (week 0) to week 14

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Explorative descriptive statistics were used for all variables. No statistical tests were performed.

| **End point values** | BT063 Placebo | BT063 50mg | BT063 100mg | Safety Set |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 12 | 12 | 12 | 36 |
| Units: subjects | 0 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Subjects with 50% Improvement of Swollen/Tender Joints or in CLASI at Week 28

| End point title | Subjects with 50% Improvement of Swollen/Tender Joints or in CLASI at Week 28 |
|---|---|

End point description:

subjects who had at least 50% improvement of swollen/tender joints or 50% improvement in CLASI score at week 28 for the ITT set

| End point type | Secondary |
|---|---|

End point timeframe:

from baseline (week 0) to week 28

| **End point values** | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10 | 11 | 12 | |
| Units: subjects | 6 | 8 | 7 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Subjects with 50% Improvement of Swollen/Tender Joints or in CLASI at Week 14

| End point title | Subjects with 50% Improvement of Swollen/Tender Joints or in CLASI at Week 14 |
|---|---|

End point description:

Subjects who had at least 50% improvement of swollen/tender joints or 50% improvement in CLASI score at week 14 for the ITT set

| End point type | Secondary |
|---|---|

End point timeframe:
From baseline (week 0) to End of Treatment Visit (week 14)

| **End point values** | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 12 | 12 | |
| Units: subjects | 6 | 7 | 7 | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Subjects with 50% Improvement in Swollen Joints at week 14**

| End point title | Subjects with 50% Improvement in Swollen Joints at week 14 |
|---|---|

End point description:
Subjects with 50% improvement in swollen joints at week 14 for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:
From baseline (week 0) to End of Treatment Visit (week 14)

| **End point values** | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 11 | 12 | 12 | |
| Units: subjects | 8 | 8 | 5 | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Subjects with 50% Improvement in Swollen Joints at week 28**

| End point title | Subjects with 50% Improvement in Swollen Joints at week 28 |
|---|---|

End point description:
subjects with 50% improvement in swollen joints  from baseline to week 28 in swollen joints for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:
From baseline (week 0) to week 28

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10 | 11 | 12 | |
| Units: subjects | 7 | 7 | 4 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects with 50% improvement in tender joints at week 14

| End point title | Subjects with 50% improvement in tender joints at week 14 |
|---|---|

End point description:

Subjects with 50% improvement in tender joints from baseline to week 14 in tender joints for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline (week 0) to End of Treatment Visit (week 14)

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 11 | 12 | 12 | |
| Units: subjects | 6 | 5 | 7 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects with 50% improvement in tender joints at week 28

| End point title | Subjects with 50% improvement in tender joints at week 28 |
|---|---|

End point description:

subjects with 50% improvement in tender joints from baseline to week 28 in tender joints for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:

from baseline (week 0) to week 28

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10 | 11 | 12 | |
| Units: subjects | 6 | 7 | 6 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects with 50% Improvement in CLASI Score at week 14

| End point title | Subjects with 50% Improvement in CLASI Score at week 14 |
|---|---|

End point description:

Subjects who had at least 50% improvement in CLASI at week 14 for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline (week 0) to End of Treatment Visit (week 14)

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 11 | 12 | 12 | |
| Units: subjects | 3 | 6 | 5 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Subjects with 50% Improvement in CLASI Score at week 28

| End point title | Subjects with 50% Improvement in CLASI Score at week 28 |
|---|---|

End point description:

Subjects who had at least 50% improvement in CLASI at week 28 for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:

from baseline (week 0) to week 28

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10 | 11 | 12 | |
| Units: subjects | 3 | 7 | 4 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: SLEDAI-2K Responders at week 14

| End point title | SLEDAI-2K Responders at week 14 |
|---|---|

End point description:

SLEDAI-2K Response was defined as subjects with more than a 3-point reduction from baseline in SLEDAI-2K score.
SLEDAI-2K Responders at week 14 for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline (week 0) to End of Treatment Visit (week 14)

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 11 | 12 | 12 | |
| Units: subjects | 4 | 5 | 4 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: SLEDAI-2K Responders at week 28

| End point title | SLEDAI-2K Responders at week 28 |
|---|---|

End point description:

SLEDAI-2K Response was defined as subjects with more than a 3-point reduction from baseline in SLEDAI-2K score.

SLEDAI-2K Responders at week 28 for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline (week 0) to week 28

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10 | 11 | 12 | |
| Units: subjects | 3 | 5 | 7 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: BILAG Response and Partial Response at week 14

| End point title | BILAG Response and Partial Response at week 14 |
|---|---|

End point description:

BILAG=British Isles Lupus Assessment Group
Response was defined as loss of "A" or "B" scores in all systems without the development of any new "A" or
"B" scores.
Partial response was defined as a loss of "A" scores but with "B" scores persisting or developing while in treatment.
Subjects with BILAG Response or Partial Response at week 14 for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline (week 0) to End of Treatment Visit (week 14)

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 11 | 12 | 12 | |
| Units: subjects | | | | |
| Response | 2 | 4 | 2 | |
| Partial Response | 6 | 3 | 8 | |
| No Response | 3 | 5 | 2 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: BILAG Response and Partial Response at week 28

| End point title | BILAG Response and Partial Response at week 28 |
|---|---|

End point description:

BILAG=British Isles Lupus Assessment Group
Response was defined as loss of "A" or "B" scores in all systems without the development of any new "A" or
"B" scores.
Partial response was defined as a loss of "A" scores but with "B" scores persisting or developing while in treatment.
Subjects with BILAG Response or Partial Response at week 28 for ITT set

| End point type | Secondary |
|---|---|

End point timeframe:
From baseline (week 0) to week 28

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10 | 11 | 12 | |
| Units: subjects | | | | |
| Response | 2 | 3 | 2 | |
| Partial Response | 6 | 5 | 8 | |
| No Response | 2 | 3 | 2 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change in ECLAM from Baseline to week 14

| End point title | Percent Change in ECLAM from Baseline to week 14 |
|---|---|

End point description:
Mean percent change from baseline in ECLAM scores at week 14

| End point type | Secondary |
|---|---|

End point timeframe:
From Baseline (week 0) to End of Treatment (week 14)

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 11 | 12 | 12 | |
| Units: percent changed score point | | | | |
| arithmetic mean (standard deviation) | -25.4 (± 32.47) | -15.5 (± 42.48) | -9.0 (± 48.05) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change in ECLAM from Baseline to week 28

| End point title | Percent Change in ECLAM from Baseline to week 28 |
|---|---|

End point description:
Mean percent change from baseline in ECLAM scores at week 28

| End point type | Secondary |
|---|---|

End point timeframe:
From baseline (week 0) to week 28

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10 | 11 | 12 | |
| Units: percent changed score point | | | | |
| arithmetic mean (standard deviation) | -1.5 (± 46.46) | -42.1 (± 41.25) | -15.9 (± 48.24) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Classified Disease Activity in Physician’s Global Assessment at week 14

| End point title | Classified Disease Activity in Physician’s Global Assessment at week 14 |
|---|---|

End point description:

The proportion of subjects with no or mild or moderate or severe disease activity at week 14.
The Physician’s Global Assessment of disease activity is based on a 100 mm visual analogue scale (VAS) with the following range and increments:

| Score | Definition |
|---|---|
| 0 | No disease activity |
| 1 | Mild disease activity |
| 2 | Moderate disease activity |
| 3 | Severe disease activity |

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline (week 0) to End of Treatment Visit (week 14)

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 12 | 12 | |
| Units: Subjects | | | | |
| No disease activity | 2 | 3 | 1 | |
| Mild disease activity | 5 | 3 | 5 | |
| Moderate disease activity | 4 | 6 | 6 | |
| Severe disease activity | 0 | 0 | 0 | |
| Missing | 1 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Classified Disease Activity in Physician's Global Assessment at Weeks 28

| End point title | Classified Disease Activity in Physician's Global Assessment at Weeks 28 |
|---|---|

End point description:

The proportion of subjects with no or mild or moderate or severe disease activity at week 28.
The Physician's Global Assessment of disease activity is based on a 100 mm visual analogue scale (VAS) with the following range and increments:

| Score | Definition |
|---|---|
| 0 | No disease activity |
| 1 | Mild disease activity |
| 2 | Moderate disease activity |
| 3 | Severe disease activity |

| End point type | Secondary |
|---|---|

End point timeframe:

From baseline (week 0) to week 28

| End point values | BT063 Placebo | BT063 50mg | BT063 100mg | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 12 | 12 | 12 | |
| Units: Subjects | | | | |
| No disease activity | 1 | 3 | 0 | |
| Mild disease activity | 6 | 5 | 8 | |
| Moderate disease activity | 3 | 3 | 3 | |
| Severe disease activity | 0 | 0 | 1 | |
| Missing | 2 | 1 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From baseline (week 0) to week 28

Adverse event reporting additional description:

An AE can be any unfavourable or unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An AE, that occurs from the first dose of study drug until week 28, is defined as a TEAE.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | BT063 Placebo |

Reporting group description:

End formulation buffer without BT063 drug product

| | |
|---|---|
| Reporting group title | BT063 50mg |

Reporting group description:

BT063 provided as a sterile solution containing the IL-10 binding monoclonal antibody (mAb)

| | |
|---|---|
| Reporting group title | BT063 100mg |

Reporting group description:

BT063 will be provided as a sterile solution containing the IL-10 binding monoclonal antibody (mAb)

| Serious adverse events | BT063 Placebo | BT063 50mg | BT063 100mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 1 / 12 (8.33%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Overdose | Additional description: Post-treatment event; Baseline Date: 01-Mar-2017;<br>Date of Last Administration: 24-May-2017;<br>AE Onset/Resolution Date: 17-Aug-2017/ 30-Aug-2017<br>Severity: moderate<br>Relationship: not related to study drug<br>Outcome: resolved | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| 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 | | | |
| Synovitis | Additional description: Post-treatment event; Baseline Date: 24-Feb-2016;<br>Date of Last Administration: 18-May-2016;<br>AE Onset/Resolution Date: 12-Jun-2016/20-Jun-2016<br>Severity: mild<br>Relationship: not related to study drug<br>Outcome: resolved | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (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 | | | |
| Bronchopneumonia | Additional description: Post-treatment event; Baseline Date: 01-Mar-2017;<br>Date of Last Administration: 24-May-2017;<br>AE Onset/Resolution Date: 27-Jul-2017/ 30-Aug-2017<br>Severity: moderate<br>Relationship: not related to study drug<br>Outcome: resolved | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | BT063 Placebo | BT063 50mg | BT063 100mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 12 (66.67%) | 4 / 12 (33.33%) | 7 / 12 (58.33%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 2 | 0 | 1 |
| Venous occlusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Tenderness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune system disorders | | | |

| | | | |
|---|---|---|---|
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract inflammat | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Complement factor decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Headache | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Mouth ulceration | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Periostitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Demodicidosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Pharyngitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 12 (8.33%) | 1 / 12 (8.33%) |
| occurrences (all) | 1 | 1 | 1 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 12 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 12 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 12 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported