



Clinical trial results:

A Phase II, Randomized, Double-blind, Placebo-controlled Study of the Safety and Efficacy of GDC-0853 in Patients with Moderate to Severe Active Systemic Lupus

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2016-001039-11 |
| Trial protocol | GB PT ES BG DE |
| Global end of trial date | 16 July 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 11 June 2020 |
| First version publication date | 11 June 2020 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | GA30044 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02908100 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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 | 16 July 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 16 July 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of GDC-0853.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy:

All Subjects were on immunosuppressants, antimalarials and/or corticosteroids.

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 19 January 2017 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 2 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects**Subjects enrolled per country**

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Argentina: 23 |
| Country: Number of subjects enrolled | Brazil: 63 |
| Country: Number of subjects enrolled | Bulgaria: 14 |
| Country: Number of subjects enrolled | Chile: 37 |
| Country: Number of subjects enrolled | Colombia: 43 |
| Country: Number of subjects enrolled | Spain: 8 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Germany: 6 |
| Country: Number of subjects enrolled | Korea, Republic of: 2 |
| Country: Number of subjects enrolled | Mexico: 14 |
| Country: Number of subjects enrolled | China: 6 |
| Country: Number of subjects enrolled | United States: 42 |
| Worldwide total number of subjects | 260 |
| EEA total number of subjects | 30 |

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) | 251 |
| From 65 to 84 years | 9 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 69 centers in 12 countries.

Pre-assignment

Screening details:

An overall total of 616 subjects were screened into the study, of which 356 subjects were screen failures. 260 subjects (Intent-To-Treat/ITT population) were randomized into the study, of which 1 subject did not receive any study treatment meaning that the Safety population consisted of 259 subjects.

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 | Investigator, Subject |

Arms

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

Arm description:

Subjects received matching placebo to GDC-0853 orally starting on Day 1 and ending at Week 48, in combination with background standard of care therapy.

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo matching GDC-0853 was administered.

| | |
|------------------|---------------------|
| Arm title | GDC-0853 (150mg) QD |
|------------------|---------------------|

Arm description:

Subjects received GDC-0853 (150mg) orally once daily (QD) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | GDC-0853 |
| Investigational medicinal product code | |
| Other name | Fenebrutinib |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

GDC-0853 was administered orally once daily (QD) at a dose of 150mg.

| | |
|--|----------|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo matching GDC-0853 was administered.

| | |
|---|----------------------|
| Arm title | GDC-0853 (200mg) BID |
| Arm description: | |
| Subjects received GDC-0853 (200mg) orally twice daily (BID) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. | |
| Arm type | Experimental |
| Investigational medicinal product name | GDC-0853 |
| Investigational medicinal product code | |
| Other name | Fenebrutinib |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

GDC-0853 was administered orally twice daily (BID) at a dose of 200mg.

| Number of subjects in period 1 | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID |
|--|---------|---------------------|----------------------|
| Started | 86 | 87 | 87 |
| Completed | 63 | 66 | 66 |
| Not completed | 23 | 21 | 21 |
| Adverse event, serious fatal | 2 | - | - |
| Non-Compliance With Contraceptive Method | 1 | - | - |
| Consent withdrawn by subject | 8 | 7 | 5 |
| Physician decision | - | 1 | - |
| Adverse event, non-fatal | 7 | 6 | 9 |
| Non-Compliance With Study Drug | 1 | 1 | 2 |
| Pregnancy | 1 | 2 | - |
| Randomised in Error | 1 | - | - |
| Lost to follow-up | - | 1 | 2 |
| Lack of efficacy | 2 | 3 | 3 |

Baseline characteristics

Reporting groups

| | |
|---|----------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received matching placebo to GDC-0853 orally starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. | |
| Reporting group title | GDC-0853 (150mg) QD |
| Reporting group description: | |
| Subjects received GDC-0853 (150mg) orally once daily (QD) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. | |
| Reporting group title | GDC-0853 (200mg) BID |
| Reporting group description: | |
| Subjects received GDC-0853 (200mg) orally twice daily (BID) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. | |

| Reporting group values | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID |
|--|---------|---------------------|----------------------|
| Number of subjects | 86 | 87 | 87 |
| Age categorical | | | |
| 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) | 83 | 83 | 85 |
| From 65-84 years | 3 | 4 | 2 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 40.2 | 43.3 | 40.4 |
| standard deviation | ± 11.5 | ± 12.4 | ± 10.6 |
| Sex: Female, Male | | | |
| Units: | | | |
| Female | 85 | 82 | 84 |
| Male | 1 | 5 | 3 |
| Race/Ethnicity, Customized | | | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 54 | 61 | 61 |
| Not Hispanic or Latino | 32 | 25 | 26 |
| Not Stated | 0 | 1 | 0 |
| Race/Ethnicity, Customized | | | |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska native | 11 | 8 | 17 |
| Asian | 7 | 1 | 2 |

| | | | |
|---------------------------|----|----|----|
| Black or African American | 11 | 15 | 13 |
| Multiple | 1 | 1 | 3 |
| White | 56 | 62 | 52 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 260 | | |
| Age categorical | | | |
| 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) | 251 | | |
| From 65-84 years | 9 | | |
| 85 years and over | 0 | | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male | | | |
| Units: | | | |
| Female | 251 | | |
| Male | 9 | | |
| Race/Ethnicity, Customized | | | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 176 | | |
| Not Hispanic or Latino | 83 | | |
| Not Stated | 1 | | |
| Race/Ethnicity, Customized | | | |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska native | 36 | | |
| Asian | 10 | | |
| Black or African American | 39 | | |
| Multiple | 5 | | |
| White | 170 | | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Placebo |
| Reporting group description: Subjects received matching placebo to GDC-0853 orally starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. | |
| Reporting group title | GDC-0853 (150mg) QD |
| Reporting group description: Subjects received GDC-0853 (150mg) orally once daily (QD) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. | |
| Reporting group title | GDC-0853 (200mg) BID |
| Reporting group description: Subjects received GDC-0853 (200mg) orally twice daily (BID) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. | |
| Subject analysis set title | Placebo (Safety-Evaluable Population) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received matching placebo to GDC-0853 orally starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. The Safety-evaluable population was defined as all participants who received at least one dose of study medication. | |
| Subject analysis set title | GDC-0853 (150mg) QD (Safety-Evaluable Population) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received GDC-0853 (150mg) orally once daily (QD) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. The Safety-evaluable population was defined as all participants who received at least one dose of study medication. | |
| Subject analysis set title | GDC-0853 (200mg) BID (Safety-Evaluable Population) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received GDC-0853 (200mg) orally twice daily (BID) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. The Safety-evaluable population was defined as all participants who received at least one dose of study medication. | |
| Subject analysis set title | Placebo (BICLA-Evaluable Population) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Subjects received matching placebo to GDC-0853 orally starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. The BICLA-evaluable population was defined as all all ITT participants who had at least one body system with moderate or severe disease activity at baseline as determined by BILAG-2004, i.e., at least one BILAG domain was scored as A or B at baseline. | |
| Subject analysis set title | GDC-0853 (150mg) QD (BICLA-Evaluable Population) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Subjects received GDC-0853 (150mg) orally once daily (QD) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. The BICLA-evaluable population was defined as all all ITT participants who had at least one body system with moderate or severe disease activity at baseline as determined by BILAG-2004, i.e., at least one BILAG domain was scored as A or B at baseline. | |
| Subject analysis set title | GDC-0853 (200mg) BID (BICLA-Evaluable Population) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: Subjects received GDC-0853 (200mg) orally twice daily (BID) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy. The BICLA-evaluable population was defined as all all ITT participants who had at least one body system with moderate or severe disease activity at baseline as determined by BILAG-2004, i.e., at least one BILAG domain was scored as A or B at baseline. | |

Primary: Systemic Lupus Erythematosus Responder Index (SRI)-4 Response at Week 48

| | |
|---|--|
| End point title | Systemic Lupus Erythematosus Responder Index (SRI)-4 Response at Week 48 |
| End point description: The Systemic Lupus Erythematosus Responder Index (SRI)-4 measures reduction in SLE disease activity and is a composite measure that includes the SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) 2004 and Physician Global Assessment. It is defined as: 1) Reduction of ≥ 4 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥ 0.3 points [10 mm] from baseline) in the Physician's Global Assessment of Disease Activity. The score range is from 0 to 100, with higher scores indicating greater disease activity. | |
| End point type | Primary |
| End point timeframe: Week 48 | |

| End point values | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86 | 87 | 87 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 44.2 | 50.6 | 51.7 | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.373 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 6.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.5 |
| upper limit | 21.2 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.339 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 7.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 22.4 |

Secondary: SRI-4 Response at Week 48 With a Sustained Reduction of Oral Corticosteroids (OCS) Dose to Less Than (<)10 Milligrams per Day (mg/day) and Less Than or Equal to (<=) Day 1 Dose During Week 36 Through Week 48

| | |
|-----------------|---|
| End point title | SRI-4 Response at Week 48 With a Sustained Reduction of Oral Corticosteroids (OCS) Dose to Less Than (<)10 Milligrams per Day (mg/day) and Less Than or Equal to (<=) Day 1 Dose During Week 36 Through Week 48 |
|-----------------|---|

End point description:

The SRI-4 measures reduction in SLE disease activity and is a composite measure that includes the SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) 2004 and Physician Global Assessment. It is defined as: 1) Reduction of ≥ 4 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥ 0.3 points [10 mm] from baseline) in the Physician's Global Assessment of Disease Activity. The score range is from 0 to 100, with higher scores indicating greater disease activity. OCS tapering requires a sustained reduction of OCS from Week 36 through Week 48 [less than 10 milligram per day (mg/day) and less or equal to the dose received on Day 1].

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

End point timeframe:

Week 48

| End point values | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86 | 87 | 87 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 41.9 | 50.6 | 44.8 | |

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.223 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 8.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.1 |
| upper limit | 23.5 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.737 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.8 |
| upper limit | 17.7 |

Secondary: SRI-4 Response at Week 24 With a Sustained Reduction of OCS Dose to < 10 mg/day and < /= Day 1 Dose During Week 12 Through Week 24

| | |
|-----------------|--|
| End point title | SRI-4 Response at Week 24 With a Sustained Reduction of OCS Dose to < 10 mg/day and < /= Day 1 Dose During Week 12 Through Week 24 |
|-----------------|--|

End point description:

The SRI-4 measures reduction in SLE disease activity and is a composite measure that includes the SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) 2004 and Physician Global Assessment. It is defined as: 1) Reduction of ≥ 4 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥ 0.3 points [10 mm] from baseline) in the Physician's Global Assessment of Disease Activity. The score range is from 0 to 100, with higher scores indicating greater disease activity. OCS tapering requires a sustained reduction of OCS from Week 12 through Week 24 [less than 10 milligram per day (mg/day) and less or equal to the dose received on Day 1].

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 24 | |

| End point values | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID | |
|-------------------------------|-----------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86 | 87 | 87 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 43.0 | 47.1 | 47.1 | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.614 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 4.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.7 |
| upper limit | 18.9 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.607 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 4.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.7 |
| upper limit | 18.9 |

Secondary: SRI-4 Response at Week 24

| | |
|-----------------|---------------------------|
| End point title | SRI-4 Response at Week 24 |
|-----------------|---------------------------|

End point description:

The Systemic Lupus Erythematosus Responder Index (SRI)-4 measures reduction in SLE disease activity and is a composite measure that includes the SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) 2004 and Physician Global Assessment. It is defined as: 1) Reduction of ≥ 4 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥ 0.3 points [10 mm] from baseline) in the Physician's Global Assessment of Disease Activity. The score range is from 0 to 100, with higher scores indicating greater disease activity.

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

End point timeframe:

Week 24

| End point values | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86 | 87 | 87 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 46.5 | 52.9 | 52.9 | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.41 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 6.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.5 |
| upper limit | 21.2 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.418 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 6.4 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.5 |
| upper limit | 21.2 |

Secondary: SRI-4 response at Week 48 in patients with high vs. low plasmablast signature levels

| | |
|---|--|
| End point title | SRI-4 response at Week 48 in patients with high vs. low plasmablast signature levels |
| End point description: The SRI-4 measures reduction in SLE disease activity and is a composite measure that includes the SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) 2004 and Physician Global Assessment. It is defined as: 1) Reduction of ≥ 4 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥ 0.3 points [10 mm] from baseline) in the Physician's Global Assessment of Disease Activity. The score range is from 0 to 100, with higher scores indicating greater disease activity. The Plasmablast Signature (PB) is a Bruton's Tyrosine Kinase (BTK)-dependent blood RNA signature comprised of three genes (IgJ, MZB1 and TXNDC5). PBS LvL = Plasmablast Signature Level. Pla (n=X); 150 (n=X) and 200 (n=X) = Number of Subjects analysed in each arm at each plasmablast signature level. | |
| End point type | Secondary |
| End point timeframe: Week 48 | |

| End point values | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID | |
|---|-------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 24 ^[1] | 24 ^[2] | 25 ^[3] | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| PBS LvL Q1 Pla (n=24); 150 (n=21); 200 (n=20) | 37.5 | 52.4 | 45.0 | |
| PBS LvL Q2 Pla (n=22); 150 (n=24); 200 (n=19) | 54.5 | 54.2 | 63.2 | |
| PBS LvL Q3 Pla (n=19); 150 (n=21); 200 (n=25) | 36.8 | 52.4 | 52.0 | |
| PBS LvL Q4 Pla (n=20); 150 (n=21); 200 (n=23) | 50.0 | 42.9 | 47.8 | |

Notes:

[1] - Data presented is only for subjects that were included in the actual analysis.

[2] - Data presented is only for subjects that were included in the actual analysis.

[3] - Data presented is only for subjects that were included in the actual analysis.

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q1 | |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.378 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 14.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14 |
| upper limit | 43.7 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q1 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.732 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 7.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.7 |
| upper limit | 36.7 |

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q2 | |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -29.2 |
| upper limit | 28.4 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q2 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.234 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 8.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.4 |
| upper limit | 38.7 |

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q3 | |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.364 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 15.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.9 |
| upper limit | 46 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q3 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.134 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 15.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.1 |
| upper limit | 44.4 |

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q4 | |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.83 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | -7.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -37.6 |
| upper limit | 23.3 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q4 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.963 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -32.1 |
| upper limit | 27.8 |

Secondary: SRI-4 response with a sustained reduction of OCS dose to ≤ 10 mg/day and \leq Day 1 dose during Week 36 through 48 in patients with high vs. low plasmablast signature levels

| | |
|-----------------|--|
| End point title | SRI-4 response with a sustained reduction of OCS dose to ≤ 10 mg/day and \leq Day 1 dose during Week 36 through 48 in patients with high vs. low plasmablast signature levels |
|-----------------|--|

End point description:

The SRI-4 measures reduction in SLE disease activity and is defined as: 1) Reduction of ≥ 4 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥ 0.3 points [10 mm] from baseline) in the Physician's Global Assessment of Disease Activity. The score range is from 0 to 100, with higher scores indicating greater disease activity. OCS tapering requires a sustained reduction of OCS from Week 36 through Week 48 [less than 10 milligram per day (mg/day) and less or equal to the dose received on Day 1]. Plasmablast Signature is a BTK-dependent blood RNA signature comprised of three genes (IgJ, MZB1 and TXNDC5). PBS LvL = Plasmablast Signature Level. Plac (n=X); 150 (n=X) and 200 (n=X) = Number of Subjects analysed in each arm at each Plasmablast Signature Level.

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

End point timeframe:

Week 48

| End point values | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID | |
|---|-------------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 24 ^[4] | 24 ^[5] | 25 ^[6] | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| PBS LvL Q1 Pla (n=24); 150 (n=21); 200 (n=20) | 33.3 | 52.4 | 40.0 | |
| PBS LvL Q2 Pla (n=22); 150 (n=24); 200 (n=19) | 54.5 | 54.2 | 57.9 | |
| PBS LvL Q3 Pla (n=19); 150 (n=21); 200 (n=25) | 36.8 | 52.4 | 44.0 | |
| PBS LvL Q4 Pla (n=20); 150 (n=21); 200 (n=23) | 45.0 | 42.9 | 39.1 | |

Notes:

[4] - Data presented is only for subjects that were included in the actual analysis.

[5] - Data presented is only for subjects that were included in the actual analysis.

[6] - Data presented is only for subjects that were included in the actual analysis.

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
|----------------------------|------------------------------------|

Statistical analysis description:

Plasmablast Signature Level Q1

| | |
|-------------------|-------------------------------|
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
|-------------------|-------------------------------|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.189 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.4 |
| upper limit | 47.5 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q1 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.909 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 6.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21.9 |
| upper limit | 35.2 |

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q2 | |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -29.2 |
| upper limit | 28.4 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q2 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.234 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 3.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -27.1 |
| upper limit | 33.8 |

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q3 | |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.364 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 15.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.9 |
| upper limit | 46 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q3 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.31 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 7.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -22 |
| upper limit | 36.3 |

| | |
|---|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q4 | |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.922 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | -2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -32.5 |
| upper limit | 28.2 |

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: Plasmablast Signature Level Q4 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 49 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.701 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | -5.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -35.4 |
| upper limit | 23.7 |

Secondary: SRI-6 Response at Week 24 and 48

| | |
|-----------------|----------------------------------|
| End point title | SRI-6 Response at Week 24 and 48 |
|-----------------|----------------------------------|

End point description:

The Systemic Lupus Erythematosus Responder Index (SRI)-6 measures reduction in SLE disease activity and is a composite measure that includes the SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) 2004 and Physician Global Assessment. It is defined as: 1) Reduction of ≥ 6 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥ 0.3 points [10 mm] from baseline) in the Physician's Global Assessment of Disease Activity. The score range is from 0 to 100, with higher scores indicating greater disease activity.

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

End point timeframe:

Week 24, 48

| End point values | Placebo | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID | |
|-------------------------------|-----------------|---------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 86 | 87 | 87 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 24 | 31.4 | 34.5 | 33.3 | |
| Week 48 | 27.9 | 39.1 | 35.6 | |

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
|----------------------------|------------------------------------|

Statistical analysis description:

Week 24

| | |
|-------------------|-------------------------------|
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
|-------------------|-------------------------------|

| | |
|---|-----|
| Number of subjects included in analysis | 173 |
|---|-----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|--|
| Analysis type | |
|---------------|--|

| | |
|---------|---------|
| P-value | = 0.692 |
|---------|---------|

| | |
|--------|-------------------------|
| Method | Cochran-Mantel-Haenszel |
|--------|-------------------------|

| | |
|--------------------|---------------------|
| Parameter estimate | Absolute Difference |
|--------------------|---------------------|

| | |
|----------------|-----|
| Point estimate | 3.1 |
|----------------|-----|

Confidence interval

| | |
|-------|------|
| level | 95 % |
|-------|------|

| | |
|-------|---------|
| sides | 2-sided |
|-------|---------|

| | |
|-------------|-------|
| lower limit | -10.9 |
|-------------|-------|

| | |
|-------------|------|
| upper limit | 17.1 |
|-------------|------|

| | |
|---|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: | |
| Week 24 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.871 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 1.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12 |
| upper limit | 15.9 |

| | |
|---|---------------------------------|
| Statistical analysis title | GDC-0853 (150mg) versus Placebo |
| Statistical analysis description: | |
| Week 48 | |
| Comparison groups | Placebo v GDC-0853 (150mg) QD |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.105 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 11.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.8 |
| upper limit | 25.1 |

| | |
|---|---------------------------------|
| Statistical analysis title | GDC-0853 (200mg) versus Placebo |
| Statistical analysis description: | |
| Week 48 | |
| Comparison groups | Placebo v GDC-0853 (200mg) BID |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.286 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 7.7 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.1 |
| upper limit | 21.6 |

Secondary: BILAG-based Composite Lupus Assessment (BICLA) Response at Week 24 and 48

| | |
|---|---|
| End point title | BILAG-based Composite Lupus Assessment (BICLA) Response at Week 24 and 48 |
| End point description: | |
| The BICLA is a composite index that is defined as follows: [1] At least one gradation of improvement in baseline BILAG scores in all body systems with moderate or severe disease activity at entry (e.g., all A (severe disease) scores falling to B (moderate), C (mild), or D (no activity) and all B scores falling to C or D; [2] No new BILAG A or more than one new BILAG B scores; [3] No worsening of total SLEDAI-2K score from baseline; [4] No significant deterioration (= <10%) in physician's global assessment and [5] No treatment failure (initiation of non-protocol treatment). | |
| End point type | Secondary |
| End point timeframe: | |
| Week 24, 48 | |

| End point values | Placebo (BICLA-Evaluable Population) | GDC-0853 (150mg) QD (BICLA-Evaluable Population) | GDC-0853 (200mg) BID (BICLA-Evaluable Population) | |
|-------------------------------|--------------------------------------|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 80 | 85 | 83 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| Week 24 | 47.5 | 45.9 | 44.6 | |
| Week 48 | 41.2 | 52.9 | 42.2 | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: | |
| Week 24 | |
| Comparison groups | Placebo (BICLA-Evaluable Population) v GDC-0853 (150mg) QD (BICLA-Evaluable Population) |
| Number of subjects included in analysis | 165 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.936 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | -1.6 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.8 |
| upper limit | 13.6 |

| | |
|---|--|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
| Statistical analysis description: | |
| Week 24 | |
| Comparison groups | Placebo (BICLA-Evaluable Population) v GDC-0853 (200mg) BID (BICLA-Evaluable Population) |
| Number of subjects included in analysis | 163 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.683 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | -2.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.2 |
| upper limit | 12.4 |

| | |
|---|---|
| Statistical analysis title | GDC-0853 (150mg) QD versus Placebo |
| Statistical analysis description: | |
| Week 48 | |
| Comparison groups | Placebo (BICLA-Evaluable Population) v GDC-0853 (150mg) QD (BICLA-Evaluable Population) |
| Number of subjects included in analysis | 165 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.086 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 11.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.4 |
| upper limit | 26.8 |

| | |
|-----------------------------------|-------------------------------------|
| Statistical analysis title | GDC-0853 (200mg) BID versus Placebo |
|-----------------------------------|-------------------------------------|

Statistical analysis description:

Week 48

| | |
|---|--|
| Comparison groups | Placebo (BICLA-Evaluable Population) v GDC-0853 (200mg) BID (BICLA-Evaluable Population) |
| Number of subjects included in analysis | 163 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.879 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute Difference |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.2 |
| upper limit | 16.1 |

Secondary: Percentage of Subjects With Adverse Events (AEs)

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Adverse Events (AEs) |
|-----------------|--|

End point description:

An Adverse Event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events.

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

End point timeframe:

Baseline up to end of study (approximately Week 60)

| End point values | Placebo (Safety-Evaluable Population) | GDC-0853 (150mg) QD (Safety-Evaluable Population) | GDC-0853 (200mg) BID (Safety-Evaluable Population) | |
|-------------------------------|---|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 84 | 87 | 88 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 76.2 | 88.5 | 78.4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of Fenebrutinib at specified timepoints

| | |
|-----------------|--|
| End point title | Plasma Concentrations of Fenebrutinib at specified timepoints ^[7] |
|-----------------|--|

End point description:

The PK analyses includes tabulation of plasma concentration data and summarisation of plasma concentrations by visits with participants grouped according to treatment received. Descriptive summary statistics includes the arithmetic mean, median, range, SD and coefficient of variation as appropriate. The PK-evaluable population was defined as all subjects who received at least one dose of fenebrutinib (GDC-0853) and had at least 1 evaluable post-dose PK sample. 999 = Not Estimable. 150 (n=X); 200 (n=X) = Number of Subjects analysed in each arm at each timepoint.

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

End point timeframe:

Baseline (Pre-dose), Week 24 (Pre-dose and Post-dose) and Week 48 (Pre-dose)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: PK Analysis was only carried out on the Treatment groups and not on the Placebo group.

| End point values | GDC-0853 (150mg) QD | GDC-0853 (200mg) BID | | |
|---|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 87 ^[8] | 86 ^[9] | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Wk 0 (Pre-dose) 150 (n=87) 200 (n=86) | 999 (± 999) | 999 (± 999) | | |
| Wk 24 (Pre-dose) 150 (n=67) 200 (n=68) | 41.9 (± 62.4) | 180 (± 121) | | |
| Wk 24 (2hr Post-dose) 150 (n=66) 200 (n=67) | 331 (± 226) | 612 (± 353) | | |
| Wk 24 (4-6hr Post-dose) 150 (n=65) 200 (n=66) | 215 (± 131) | 414 (± 187) | | |
| Wk 24 (8-10hr Post-dose) 150 (n=11) 200 (n=7) | 120 (± 111) | 233 (± 145) | | |
| Week 48 (Pre-dose) 150 (n=64) 200 (n=64) | 25.5 (± 28.1) | 137 (± 133) | | |

Notes:

[8] - Data presented is only for subjects that were included in the actual analysis.

[9] - Data presented is only for subjects that were included in the actual analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2 years, 6 months

Adverse event reporting additional description:

The safety population was defined as all subjects who received at least one dose of study medication. AEs that were entered into the database at the time of the database lock were included in the AE analysis.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | GDC-0853 (150mg) QD |
|-----------------------|---------------------|

Reporting group description:

Subjects received GDC-0853 (150mg) orally once daily (QD) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy.

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

Reporting group description:

Subjects received matching placebo to GDC-0853 orally twice daily (BID) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy.

| | |
|-----------------------|----------------------|
| Reporting group title | GDC-0853 (200mg) BID |
|-----------------------|----------------------|

Reporting group description:

Subjects received GDC-0853 (200mg) orally twice daily (BID) starting on Day 1 and ending at Week 48, in combination with background standard of care therapy.

| Serious adverse events | GDC-0853 (150mg) QD | Placebo | GDC-0853 (200mg) BID |
|---|---------------------|-----------------|----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 87 (4.60%) | 9 / 84 (10.71%) | 12 / 88 (13.64%) |
| number of deaths (all causes) | 1 | 2 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CERVIX CARCINOMA STAGE 0 | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SALIVARY GLAND NEOPLASM | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 84 (0.00%) | 0 / 88 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |

| | | | |
|--|----------------|----------------|----------------|
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| Surgical and medical procedures | | | |
| ABORTION INDUCED | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 84 (0.00%) | 0 / 88 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| ABORTION SPONTANEOUS | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| General disorders and administration site conditions | | | |
| MULTIPLE ORGAN DYSFUNCTION SYNDROME | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| ACUTE RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| PULMONARY OEDEMA | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| RESPIRATORY FAILURE | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Psychiatric disorders | | | |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 | | | |
| ANKLE FRACTURE | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| CONGESTIVE CARDIOMYOPATHY | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| MYOCARDITIS | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| SYNCOPE | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| LEUKOCYTOSIS | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 84 (0.00%) | 0 / 88 (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 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| SKIN ULCER | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| Renal and urinary disorders | | | |
| RENAL COLIC | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL IMPAIRMENT | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| 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 | | | |
| CHEST WALL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| MUSCULAR WEAKNESS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYSTEMIC LUPUS ERYTHEMATOSUS | | | |
| subjects affected / exposed | 1 / 87 (1.15%) | 2 / 84 (2.38%) | 2 / 88 (2.27%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| EPSTEIN-BARR VIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| GASTROENTERITIS BACTERIAL | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| INFECTED SKIN ULCER | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| OSTEOMYELITIS CHRONIC | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (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 |
| PULMONARY TUBERCULOSIS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 87 (1.15%) | 0 / 84 (0.00%) | 0 / 88 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYELONEPHRITIS | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 0 / 88 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 87 (0.00%) | 1 / 84 (1.19%) | 1 / 88 (1.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | GDC-0853 (150mg) QD | Placebo | GDC-0853 (200mg) BID |
|---|------------------------|------------------|-------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 54 / 87 (62.07%) | 42 / 84 (50.00%) | 51 / 88 (57.95%) |
| Nervous system disorders | | | |
| HEADACHE | | | |
| subjects affected / exposed | 3 / 87 (3.45%) | 9 / 84 (10.71%) | 3 / 88 (3.41%) |
| occurrences (all) | 4 | 10 | 3 |
| Blood and lymphatic system disorders | | | |
| LYMPHOPENIA | | | |
| subjects affected / exposed | 2 / 87 (2.30%) | 6 / 84 (7.14%) | 10 / 88 (11.36%) |
| occurrences (all) | 2 | 6 | 12 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 5 / 87 (5.75%) | 4 / 84 (4.76%) | 6 / 88 (6.82%) |
| occurrences (all) | 5 | 5 | 6 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN UPPER | | | |

| | | | |
|---|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 2 / 87 (2.30%) 2 | 1 / 84 (1.19%) 1 | 5 / 88 (5.68%) 7 |
| DIARRHOEA subjects affected / exposed occurrences (all) | 5 / 87 (5.75%) 8 | 6 / 84 (7.14%) 6 | 5 / 88 (5.68%) 6 |
| NAUSEA subjects affected / exposed occurrences (all) | 4 / 87 (4.60%) 4 | 7 / 84 (8.33%) 7 | 7 / 88 (7.95%) 7 |
| Skin and subcutaneous tissue disorders RASH subjects affected / exposed occurrences (all) | 3 / 87 (3.45%) 3 | 0 / 84 (0.00%) 0 | 6 / 88 (6.82%) 8 |
| Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) | 1 / 87 (1.15%) 1 | 2 / 84 (2.38%) 4 | 5 / 88 (5.68%) 6 |
| BACK PAIN subjects affected / exposed occurrences (all) | 8 / 87 (9.20%) 9 | 2 / 84 (2.38%) 3 | 4 / 88 (4.55%) 4 |
| Infections and infestations BRONCHITIS subjects affected / exposed occurrences (all) | 6 / 87 (6.90%) 6 | 6 / 84 (7.14%) 7 | 7 / 88 (7.95%) 9 |
| GASTROENTERITIS subjects affected / exposed occurrences (all) | 2 / 87 (2.30%) 2 | 5 / 84 (5.95%) 7 | 2 / 88 (2.27%) 2 |
| INFLUENZA subjects affected / exposed occurrences (all) | 5 / 87 (5.75%) 5 | 5 / 84 (5.95%) 8 | 5 / 88 (5.68%) 5 |
| NASOPHARYNGITIS subjects affected / exposed occurrences (all) | 8 / 87 (9.20%) 12 | 5 / 84 (5.95%) 6 | 6 / 88 (6.82%) 6 |
| SINUSITIS subjects affected / exposed occurrences (all) | 2 / 87 (2.30%) 2 | 3 / 84 (3.57%) 3 | 5 / 88 (5.68%) 5 |
| UPPER RESPIRATORY TRACT INFECTION | | | |

| | | | |
|-----------------------------|------------------|-----------------|------------------|
| subjects affected / exposed | 9 / 87 (10.34%) | 5 / 84 (5.95%) | 3 / 88 (3.41%) |
| occurrences (all) | 10 | 7 | 3 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 17 / 87 (19.54%) | 9 / 84 (10.71%) | 11 / 88 (12.50%) |
| occurrences (all) | 21 | 11 | 15 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 12 May 2017 | Following updates were made: [1] Better characterisation of Primary SRI-4 endpoint, addition of an endpoint to better capture changes in skin and joint domains and endpoint has been added to assess improvement in Patient's Global Assessment at Weeks 24 and 48; [2] Extension of Screening period from 28 to 35 days; [3] Clarification of language on angiotensin converting enzyme inhibitors and angiotensin receptor blockers, steroid burst treatment and the SELENA-SLEDAI disease activity index being updated to SLEDAI-2K; [4] Update to timing of Interim analysis; [5] Updates to Eligibility criteria; [6] Clarification of language relating to dosing schedules, site responsibilities, injections of corticosteroids and dosage of antimalarials; [7] Update to Prohibited Therapies section; [8] Clarification of language around fasting requirements, requirements for chest radiography, SLE disease activity instruments, endpoints, training requirements and clinical manifestations, laboratory tests and reporting of terms and events; [9] Updates made to the Statistical Considerations and Analysis Plan and Schedule of Assessments and [10] Further updates made to the Appendices and Indexes. |
| 09 February 2018 | Following updates were made: [1] Modification to the Study Design Figure; [2] Updates and re-categorisation to SRI secondary efficacy endpoints; [3] Updates to PK objectives and endpoints; [4] Clarification to language for nonclinical efficacy data for the BTK inhibitor GDC-0834; [5] Update to minimum SLEDAI-2K score requirement for subjects to enrol in the study; [6] Updates to Inclusion/Exclusion criteria; [7] Updates to language regarding study drug administration, dosage and steroid burst treatment and tapering; [8] Updates to the Prohibited Therapies section and [9] Other updates including to the Hepatotoxicity language, analysis for Primary endpoint and PK, measurements to be carried out at Week 48 and PD Biomarkers. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported