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