Clinical trial results:
A Phase II, Randomized, Double-blind, Placebo-controlled Dose-ranging Study to Evaluate the Safety and Efficacy of M2951 in Subjects with SLE

Summary

EudraCT number	2016-002950-19
Trial protocol	BG PL DE RO
Global end of trial date	23 March 2020

Results information

Result version number	v1 (current)
This version publication date	01 April 2021
First version publication date	01 April 2021

Trial information

Trial identification

Sponsor protocol code	MS200527-0018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02975336
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck KGaA, Darmstadt, Germany
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Communication Centre, Merck KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com
Scientific contact	Communication Center, Merck KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.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	23 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2019
Global end of trial reached?	Yes
Global end of trial date	23 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to evaluate the efficacy and dose response of evobrutinib compared with placebo in reducing disease activity in adult subjects with active, autoantibody-positive Systemic Lupus Erythematosus (SLE) who received Standard of Care therapy based on systemic lupus erythematosus responder index (SRI-4) response at Week 52 in all subjects, or on SRI-6 response at Week 52 in the high disease activity (HDA) subgroup, defined as Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) greater than or equal to (>=)10.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 27
Country: Number of subjects enrolled	Colombia: 41
Country: Number of subjects enrolled	Mauritius: 18
Country: Number of subjects enrolled	Peru: 43
Country: Number of subjects enrolled	South Africa: 23
Country: Number of subjects enrolled	United States: 89
Country: Number of subjects enrolled	Japan: 20
Country: Number of subjects enrolled	Bulgaria: 48
Country: Number of subjects enrolled	Chile: 22
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Mexico: 42
Country: Number of subjects enrolled	Philippines: 26
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Romania: 1

Country: Number of subjects enrolled	Italy: 9
Worldwide total number of subjects	469
EEA total number of subjects	87

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)	458
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Primary and Secondary endpoints were planned to be analyze only for Double-Blind Placebo-controlled period.

Pre-assignment

Screening details:

A total of 1053 subjects with SLE were screened. Out of which, 469 subjects were randomized in ratio of 1:1:1:1 to 1 of 4 treatment groups: Placebo; M2951 25mg QD, M2951 75 mg QD and M2951 50 mg BID. 283 out of 348 subjects that completed Double-Blind Placebo-Controlled (DBPC) period, entered the Long-Term Extension (LTE) period of study.

Period 1

Period 1 title	DBPC (52 weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	DBPC: Placebo

Arm description:

Subjects received placebo matched to M2951 orally for 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to M2951 orally for 52 weeks.

Arm title	DBPC: M2951 25 mg QD

Arm description:

Subjects received 25 milligrams (mg) of M2951 orally once daily (QD) for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Evobrutinib
Investigational medicinal product code	M2951
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 25 mg of M2951 orally QD for 52 weeks.

Arm title	DBPC: M2951 75 mg QD

Arm description:

Subjects received 75 mg of M2951 orally QD for 52 weeks.

Arm type	Experimental

Investigational medicinal product name	Evobrutinib
Investigational medicinal product code	M2951
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 75 mg of M2951 orally QD for 52 weeks.

Arm title	DBPC: M2951 50 mg BID

Arm description:

Subjects received 50 mg of M2951 orally twice daily (BID) for 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Evobrutinib
Investigational medicinal product code	M2951
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 50 mg of M2951 orally BID for 52 weeks.

Number of subjects in period 1	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD
Started	117	118	117
Completed	85	89	90
Not completed	32	29	27
Consent withdrawn by subject	1	-	1
Premature termination of the study	5	6	6
Adverse event, non-fatal	16	17	13
Lost to follow-up	2	1	2
Protocol deviation	4	1	3
Lack of efficacy	4	4	2

Number of subjects in period 1	DBPC: M2951 50 mg BID
Started	117
Completed	84
Not completed	33
Consent withdrawn by subject	3
Premature termination of the study	4
Adverse event, non-fatal	18
Lost to follow-up	4
Protocol deviation	1
Lack of efficacy	3

Period 2

Period 2 title	LTE (104 weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	LTE: Placebo/ M2951 50 mg BID

Arm description:

Subjects who received Placebo in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.

Arm type	Experimental
Investigational medicinal product name	Evobrutinib
Investigational medicinal product code	M2951
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who received Placebo in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.

Arm title	LTE: M2951 25 mg QD/ M2951 50 mg BID

Arm description:

Subjects who received 25 mg of M2951 orally QD in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.

Arm type	Experimental
Investigational medicinal product name	Evobrutinib
Investigational medicinal product code	M2951
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who received 25 mg of M2951 orally QD in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.

Arm title	LTE: M2951 75 mg QD/ M2951 50 mg BID

Arm description:

Subjects who received 75 mg of M2951 orally QD in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.

Arm type	Experimental
Investigational medicinal product name	Evobrutinib
Investigational medicinal product code	M2951
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who received 75 mg of M2951 orally QD in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.

Arm title	LTE: M2951 50 mg BID/ M2951 50 mg BID

Arm description:

Subjects who received 50 mg of M2951 orally BID in DBPC period continued to receive same dose of M2951 orally BID in LTE period for 104 weeks.

Arm type	Experimental
Investigational medicinal product name	Evobrutinib
Investigational medicinal product code	M2951
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who received 50 mg of M2951 orally BID in DBPC period continued to receive same dose of M2951 orally BID in LTE period for 104 weeks.

Number of subjects in period 2[1]	LTE: Placebo/ M2951 50 mg BID	LTE: M2951 25 mg QD/ M2951 50 mg BID	LTE: M2951 75 mg QD/ M2951 50 mg BID
Started	62	69	80
Completed	0	0	0
Not completed	62	69	80
Adverse event, non-fatal	7	4	2
Lost to follow-up	-	1	-
unspecified	55	63	76
Lack of efficacy	-	1	2

Number of subjects in period 2[1]	LTE: M2951 50 mg BID/ M2951 50 mg BID
Started	72
Completed	0
Not completed	72
Adverse event, non-fatal	-
Lost to follow-up	-
unspecified	72
Lack of efficacy	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only 283 subjects from Double-Blind Placebo-Controlled continued in the Long-Term Extension Period.

Baseline characteristics

Reporting groups	
Reporting group title	DBPC: Placebo
Reporting group description:	
Subjects received placebo matched to M2951 orally for 52 weeks.	
Reporting group title	DBPC: M2951 25 mg QD
Reporting group description:	
Subjects received 25 milligrams (mg) of M2951 orally once daily (QD) for 52 weeks.	
Reporting group title	DBPC: M2951 75 mg QD
Reporting group description:	
Subjects received 75 mg of M2951 orally QD for 52 weeks.	
Reporting group title	DBPC: M2951 50 mg BID
Reporting group description:	
Subjects received 50 mg of M2951 orally twice daily (BID) for 52 weeks.	

Reporting group values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD
Number of subjects	117	118	117
Age categorical Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	40.2	38.8	41.5
standard deviation	± 12.49	± 12.45	± 12.52
Sex: Female, Male Units: Subjects			
Female	110	112	111
Male	7	6	6
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	23	17	21
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	10	12	11
White	66	73	68
More than one race	0	0	0
Unknown or Not Reported	18	16	17
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	45	51	47
Not Hispanic or Latino	72	67	70
Unknown or Not Reported	0	0	0

Reporting group values	DBPC: M2951 50 mg BID	Total	
Number of subjects	117	469	

Age categorical Units: Subjects			

Age Continuous Units: Years			
arithmetic mean	42.2		
standard deviation	± 11.78	-	
Sex: Female, Male Units: Subjects			
Female	112	445	
Male	5	24	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	13	74	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	12	45	
White	83	290	
More than one race	0	0	
Unknown or Not Reported	9	60	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	42	185	
Not Hispanic or Latino	75	284	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	DBPC: Placebo
Reporting group description:	
Subjects received placebo matched to M2951 orally for 52 weeks.	
Reporting group title	DBPC: M2951 25 mg QD
Reporting group description:	
Subjects received 25 milligrams (mg) of M2951 orally once daily (QD) for 52 weeks.	
Reporting group title	DBPC: M2951 75 mg QD
Reporting group description:	
Subjects received 75 mg of M2951 orally QD for 52 weeks.	
Reporting group title	DBPC: M2951 50 mg BID
Reporting group description:	
Subjects received 50 mg of M2951 orally twice daily (BID) for 52 weeks.	
Reporting group title	LTE: Placebo/ M2951 50 mg BID
Reporting group description:	
Subjects who received Placebo in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.	
Reporting group title	LTE: M2951 25 mg QD/ M2951 50 mg BID
Reporting group description:	
Subjects who received 25 mg of M2951 orally QD in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.	
Reporting group title	LTE: M2951 75 mg QD/ M2951 50 mg BID
Reporting group description:	
Subjects who received 75 mg of M2951 orally QD in DBPC period were switched to receive 50 mg M2951 orally BID in LTE period for 104 weeks.	
Reporting group title	LTE: M2951 50 mg BID/ M2951 50 mg BID
Reporting group description:	
Subjects who received 50 mg of M2951 orally BID in DBPC period continued to receive same dose of M2951 orally BID in LTE period for 104 weeks.	

Primary: DBPC: Number of Subjects With Response Based on Systemic Lupus Erythematosus Responder Index 4 (SRI-4) at Week 52

End point title	DBPC: Number of Subjects With Response Based on Systemic Lupus Erythematosus Responder Index 4 (SRI-4) at Week 52
End point description:	
SRI-4 response was defined as >= 4-point reduction in SLEDAI-2K total score, no new British Isles Lupus Assessment Group (BILAG) A and no more than 1 new BILAG B domain score, no worsening (less than 10 percent increase) from baseline in Physician's Global Assessment of Disease Activity (PGA) and no treatment failure. SLEDAI-2K assessment consists of 24 items with total score of 0(no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE divided into 9 organ systems. For each organ system A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. The PGA assess disease activity on a visual analogue scale =from 0(very well) to 100(very poor). The mITT analysis population was used.	
End point type	Primary
End point timeframe:	
Week 52	

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	115	116	114
Units: Subjects	52	64	60	55

Statistical analyses

Statistical analysis title	Placebo and M2951 25mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	2.64

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	2.18

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID

Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.93

Primary: DBPC: Number of Subjects With Response Based on Systemic Lupus Erythematosus Responder Index 6 (SRI-6) at Week 52

End point title	DBPC: Number of Subjects With Response Based on Systemic Lupus Erythematosus Responder Index 6 (SRI-6) at Week 52

End point description:

SRI-6 response was defined as >= 6-point reduction in SLEDAI-2K total score, no new BILAG A and no more than 1 new BILAG B domain score and no worsening (less than 10 percent increase) from baseline in PGA of disease activity and treatment failure. SLEDAI-2K assessment consists of 24 items with total score of 0 (no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system :A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. The PGA assess disease activity on a visual analogue scale =from 0(very well) to 100(very poor). The mITT analysis set was used. Here, "Number of subjects analyzed" signifies High Disease Activity (HDA) subgroup who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	54	65	55
Units: Subjects	22	27	30	24

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD

Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	3.24

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	2.97

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	2.75

Primary: DBPC: Number of Subjects With Treatment-Emergent Adverse Events

(TEAEs) and Serious TEAEs According to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 4.03 (NCI-CTCAE v4.03)

End point title	DBPC: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious TEAEs According to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 4.03 (NCI-CTCAE v4.03)[1]

End point description:

Adverse event (AE) was defined as any untoward medical occurrence in a subject, which does not necessarily have causal relationship with treatment. A serious AE was defined as an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged in subject hospitalization; congenital anomaly/birth defect or was otherwise considered medically important. TEAEs: events between first dose of study drug that were absent before treatment/that worsened relative to pre-treatment state up to 56 weeks. TEAEs included both serious TEAEs and non-serious TEAEs. Number of subjects with TEAEs and serious TEAEs were reported. The safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo).

End point type	Primary

End point timeframe:

Baseline up to Week 56

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	118	117	117
Units: Subjects				
Any TEAEs	96	103	100	99
Any serious TEAE	10	13	11	9

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) by Severity According to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 4.03 (NCI-CTCAE v4.03)

End point title	DBPC: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) by Severity According to National Cancer Institute-Common Terminology Criteria for Adverse Events Version 4.03 (NCI-CTCAE v4.03)[2]

End point description:

Severity of TEAEs were graded using NCI-CTCAE v4.03 toxicity grades, as follows: Grade 1= Mild; Grade 2 = Moderate; Grade 3 = Severe; Grade 4 = Life-threatening and Grade 5 = Death. Number of subjects with TEAEs by severity were reported. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo).

End point type	Primary

End point timeframe:

Baseline up to Week 56

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	118	117	117
Units: Subjects				
Grade 1	76	80	79	76
Grade 2	63	77	72	78
Grade 3	24	29	24	21
Grade 4	1	1	0	2
Grade 5	0	1	1	0

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Number of Subjects With Clinically Significant Change From Baseline in Vital Signs

End point title	DBPC: Number of Subjects With Clinically Significant Change From Baseline in Vital Signs[3]

End point description:

Vital signs included body temperature, systolic and diastolic blood pressure, pulse rate, respiratory rate, weight and height. Clinical significance was determined by the investigator. The number of subjects with clinically significant changes from baseline in vital signs were reported. The safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo).

End point type	Primary

End point timeframe:

Baseline up to Week 56

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	118	117	117
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Number of Subjects With Clinically Significant Changes From Baseline in 12-Lead Electrocardiogram (ECG) Findings

End point title	DBPC: Number of Subjects With Clinically Significant Changes From Baseline in 12-Lead Electrocardiogram (ECG) Findings[4]

End point description:

12-lead ECG recordings included rhythm, heart rate (as measured by RR interval), PR interval, QRS duration, and QT interval. The corrected QT interval (QTcF) was calculated using Fridericia's formula. 12-lead ECG recordings were obtained after the subjects have rested for at least 10 minutes in

semisupine position. Clinical significance was determined by the investigator. The number of subjects with clinically significant changes from baseline in 12-lead ECG findings were reported. The safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo).

End point type	Primary

End point timeframe:

Baseline up to Week 56

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	118	117	117
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Number of Subjects With Clinically Significant Changes From Baseline in Laboratory Parameters

End point title	DBPC: Number of Subjects With Clinically Significant Changes From Baseline in Laboratory Parameters[5]

End point description:

Laboratory investigation included hematology, biochemistry, urinalysis and coagulation. Clinical significance was determined by the investigator. The number of subjects with clinically significant changes from baseline in laboratory parameters were reported. The safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo).

End point type	Primary

End point timeframe:

Baseline up to Week 56

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	117	118	117	117
Units: Subjects	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 2

End point title	DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 2[6]

End point description:

Mean absolute value of serum levels of IgG, IgA, IgM were assessed at Week 2. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 2

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	116	115	113
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	14.56 (± 5.367)	13.75 (± 4.652)	14.37 (± 5.536)	12.81 (± 3.847)
IgA	2.62 (± 1.207)	2.75 (± 1.374)	2.78 (± 1.328)	2.66 (± 1.137)
IgM	1.12 (± 0.662)	1.22 (± 0.890)	1.09 (± 0.697)	1.18 (± 0.776)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 4

End point title	DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 4[7]

End point description:

Mean absolute value of serum levels of IgG, IgA, IgM were assessed at Week 4. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 4

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	114	114	115
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	14.92 (± 5.497)	13.60 (± 4.590)	14.21 (± 4.828)	12.73 (± 3.771)

IgA	2.71 (± 1.284)	2.73 (± 1.349)	2.82 (± 1.293)	2.64 (± 1.109)
IgM	1.12 (± 0.699)	1.18 (± 0.824)	1.06 (± 0.676)	1.16 (± 0.745)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 12

End point title	DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 12[8]

End point description:

Mean absolute value of serum levels of IgG, IgA, IgM were assessed at Week 12. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 12

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	106	110	105
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG:	14.91 (± 5.312)	12.92 (± 4.332)	13.64 (± 4.035)	12.38 (± 3.520)
IgA	2.72 (± 1.321)	2.73 (± 1.340)	2.88 (± 1.363)	2.68 (± 1.021)
IgM	1.11 (± 0.683)	1.05 (± 0.700)	0.95 (± 0.610)	1.02 (± 0.695)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 24

End point title	DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 24[9]

End point description:

Mean absolute value of serum levels of IgG, IgA, IgM were assessed at Week 24. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 24

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	101	96
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	15.01 (± 5.190)	13.75 (± 4.783)	13.79 (± 4.165)	12.86 (± 3.725)
IgA	2.79 (± 1.430)	2.89 (± 1.460)	2.98 (± 1.391)	2.78 (± 1.091)
IgM	1.07 (± 0.609)	1.01 (± 0.686)	0.89 (± 0.583)	0.98 (± 0.656)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 36

End point title	DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 36[10]

End point description:

Mean absolute value of serum levels of IgG, IgA, IgM were assessed at Week 36. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 36

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	91	97	86
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	14.81 (± 5.217)	13.54 (± 4.242)	13.67 (± 3.934)	12.65 (± 3.480)
IgA	2.72 (± 1.378)	2.89 (± 1.418)	3.01 (± 1.420)	2.86 (± 1.073)
IgM	1.06 (± 0.630)	1.01 (± 0.669)	0.85 (± 0.541)	0.95 (± 0.656)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 52

End point title	DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 52[11]

End point description:

Mean absolute value of serum levels of IgG, IgA, IgM were assessed at Week 52. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for the specified category.

End point type	Primary

End point timeframe:

Week 52

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	83	85	76
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG: n= 78, 83, 85, 76	15.21 (± 5.105)	13.90 (± 4.087)	14.32 (± 4.542)	13.01 (± 3.723)
IgA: n= 78, 83, 85, 76	2.82 (± 1.438)	2.95 (± 1.596)	3.17 (± 1.596)	2.95 (± 1.159)
IgM: n= 78, 83, 84, 76	1.08 (± 0.624)	0.94 (± 0.645)	0.82 (± 0.487)	0.96 (± 0.670)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 56

End point title	DBPC: Mean Absolute Value of Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 56[12]

End point description:

Mean absolute value of serum levels of IgG, IgA, IgM were assessed at Week 56. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 56

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	36	31	33
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	14.82 (± 5.504)	14.25 (± 4.435)	14.25 (± 4.626)	13.12 (± 4.507)
IgA	2.95 (± 1.549)	3.01 (± 1.459)	2.89 (± 1.655)	3.03 (± 1.164)
IgM	1.11 (± 0.642)	1.01 (± 0.601)	0.95 (± 0.624)	1.31 (± 0.869)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Total B Cell Count at Week 4

End point title	DBPC: Mean Absolute Total B Cell Count at Week 4[13]

End point description:

Mean total B cell count were assessed. Flow cytometry analysis of lymphocyte populations using four-color fluorescence activated cell sorting was performed for the analysis of B cell counts. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 4

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	99	99	99
Units: Cells per microliter				
arithmetic mean (standard deviation)	150 (± 126.9)	236 (± 197.4)	296 (± 243.8)	229 (± 232.9)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Total B Cell Count at Week 24

End point title	DBPC: Mean Absolute Total B Cell Count at Week 24[14]

End point description:

Mean absolute total B cell count were assessed. Flow cytometry analysis of lymphocyte populations using four-color fluorescence activated cell sorting was performed for the analysis of B cell counts. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 24

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	89	90	87	88
Units: Cells per microliter				
arithmetic mean (standard deviation)	161 (± 125.8)	184 (± 152.6)	204 (± 158.3)	151 (± 129.2)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Total B Cell Count at Week 52

End point title	DBPC: Mean Absolute Total B Cell Count at Week 52[15]

End point description:

Mean absolute total B cell count were assessed. Flow cytometry analysis of lymphocyte populations using four-color fluorescence activated cell sorting was performed for the analysis of B cell counts. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 52

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	66	76	66
Units: Cells per microliter				
arithmetic mean (standard deviation)	169 (± 121.9)	167 (± 168.7)	180 (± 170.7)	119 (± 84.1)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Mean Absolute Total B Cell Count at Week 56

End point title	DBPC: Mean Absolute Total B Cell Count at Week 56[16]

End point description:

Mean absolute total B cell count were assessed. Flow cytometry analysis of lymphocyte populations using four-color fluorescence activated cell sorting was performed for the analysis of B cell counts. The

Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Week 56

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	30	27	30
Units: Cells per microliter				
arithmetic mean (standard deviation)	164 (± 113.3)	129 (± 100.0)	156 (± 127.1)	104 (± 71.9)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 2

End point title	DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 2[17]

End point description:

Change from baseline in the serum levels of IgG, IgA, IgM were assessed. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 2

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	116	115	113
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	-0.51 (± 1.726)	-0.06 (± 1.361)	-0.15 (± 1.772)	-0.40 (± 1.025)
IgA	-0.11 (± 0.435)	-0.04 (± 0.431)	-0.01 (± 0.381)	-0.03 (± 0.268)
IgM	0.00 (± 0.197)	-0.05 (± 0.194)	-0.04 (± 0.155)	-0.07 (± 0.116)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 4

End point title	DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 4[18]

End point description:

Change from baseline in the serum levels of IgG, IgA, IgM were assessed. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 4

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	114	114	115
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	-0.26 (± 1.760)	-0.16 (± 1.463)	-0.24 (± 1.657)	-0.45 (± 1.150)
IgA	-0.01 (± 0.205)	-0.04 (± 0.334)	0.03 (± 0.447)	-0.03 (± 0.301)
IgM	0.01 (± 0.195)	-0.09 (± 0.175)	-0.07 (± 0.192)	-0.08 (± 0.159)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 12

End point title	DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 12[19]

End point description:

Change from baseline in the serum levels of IgG, IgA, IgM were assessed. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 12

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	106	110	105
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	-0.36 (± 2.073)	-0.62 (± 1.827)	-0.72 (± 2.552)	-0.93 (± 1.640)
IgA	0.00 (± 0.325)	-0.02 (± 0.360)	0.06 (± 0.518)	-0.03 (± 0.340)
IgM	-0.01 (± 0.194)	-0.20 (± 0.301)	-0.18 (± 0.277)	-0.20 (± 0.250)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 24

End point title	DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 24[20]

End point description:

Change from baseline in the serum levels of IgG, IgA, IgM were assessed. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 24

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	97	101	96
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	-0.21 (± 2.318)	0.11 (± 2.234)	-0.46 (± 2.912)	-0.57 (± 2.363)
IgA	0.06 (± 0.332)	0.14 (± 0.390)	0.19 (± 0.565)	0.04 (± 0.563)
IgM	-0.01 (± 0.264)	-0.23 (± 0.369)	-0.23 (± 0.321)	-0.25 (± 0.346)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 36

End point title	DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 36[21]

End point description:

Change from baseline in the serum levels of IgG, IgA, IgM were assessed. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 36

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	91	97	86
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	-0.15 (± 2.130)	0.02 (± 2.487)	-0.43 (± 2.572)	-0.69 (± 2.189)
IgA	-0.02 (± 0.361)	0.22 (± 0.453)	0.24 (± 0.583)	0.08 (± 0.459)
IgM	-0.04 (± 0.255)	-0.25 (± 0.416)	-0.25 (± 0.284)	-0.28 (± 0.392)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 52

End point title	DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 52[22]

End point description:

Change from baseline in the serum levels of IgG, IgA, IgM were assessed. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint and "n" signified those subjects who were evaluable for the specified category.

End point type	Primary

End point timeframe:

Baseline and Week 52

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78	83	85	76
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG: n= 78, 83, 85, 76	0.41 (± 2.898)	0.29 (± 2.361)	0.35 (± 2.688)	-0.31 (± 2.344)
IgA: n= 78, 83, 85, 76	0.19 (± 0.420)	0.32 (± 0.492)	0.39 (± 0.767)	0.18 (± 0.469)
IgM: n= 78, 83, 84, 76	-0.02 (± 0.235)	-0.25 (± 0.303)	-0.21 (± 0.318)	-0.33 (± 0.456)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 56

End point title	DBPC: Change From Baseline in Serum Immunoglobulin (Ig) Levels (IgG, IgA, IgM) at Week 56[23]

End point description:

Change from baseline in the serum levels of IgG, IgA, IgM were assessed. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 56

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	36	31	33
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)				
IgG	0.74 (± 2.907)	1.06 (± 2.607)	0.74 (± 1.987)	-0.40 (± 2.823)
IgA	0.23 (± 0.468)	0.48 (± 0.600)	0.35 (± 0.488)	0.26 (± 0.498)
IgM	0.01 (± 0.266)	-0.15 (± 0.219)	-0.11 (± 0.225)	-0.21 (± 0.488)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Total B Cell Count at Week 4

End point title	DBPC: Change From Baseline in Total B Cell Count at Week

End point description:

Change from baseline in Total B cell count were assessed. Flow cytometry analysis of lymphocyte populations using four-color fluorescence-activated cell sorting was performed for the analysis of B cell counts. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 4

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	88	88	91
Units: Cells per microliter				
arithmetic mean (standard deviation)	-5 (± 93.7)	65 (± 146.6)	87 (± 146.2)	67 (± 109.1)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Total B Cell Count at Week 24

End point title	DBPC: Change From Baseline in Total B Cell Count at Week

End point description:

Change from baseline in Total B cell count were assessed. Flow cytometry analysis of lymphocyte populations using four-color fluorescence-activated cell sorting was performed for the analysis of B cell counts. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 24

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	82	73	81
Units: Cells per microliter				
arithmetic mean (standard deviation)	2 (± 98.1)	5 (± 112.0)	3 (± 103.2)	-7 (± 134.7)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Total B Cell Count at Week 52

End point title	DBPC: Change From Baseline in Total B Cell Count at Week

End point description:

Change from baseline in Total B cell count were assessed. Flow cytometry analysis of lymphocyte populations using four-color fluorescence-activated cell sorting was performed for the analysis of B cell counts. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 52

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	57	60	63	60
Units: Cells per microliter				
arithmetic mean (standard deviation)	-14 (± 103.0)	-19 (± 133.3)	-14 (± 147.5)	-52 (± 215.7)

Statistical analyses

No statistical analyses for this end point

Primary: DBPC: Change From Baseline in Total B Cell Count at Week 56

End point title	DBPC: Change From Baseline in Total B Cell Count at Week

End point description:

Change from baseline in Total B cell count were assessed. Flow cytometry analysis of lymphocyte populations using four-color fluorescence-activated cell sorting was performed for the analysis of B cell counts. The Safety analysis set included all subjects who received at least one dose of IMP (Evobrutinib or Placebo). Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Primary

End point timeframe:

Baseline and Week 56

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned for this endpoint.

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	27	24	24
Units: Cells per microliter				
arithmetic mean (standard deviation)	7 (± 96.2)	-70 (± 138.2)	-75 (± 192.1)	-48 (± 85.8)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Time to First Severe British Isles Lupus Assessment Group (BILAG) A Flare

End point title	DBPC: Time to First Severe British Isles Lupus Assessment Group (BILAG) A Flare

End point description:

BILAG Index:assessing clinical signs,symptoms,laboratory parameters related to SLE,divided into 9 organ systems.For each organ system based on alphabetic score:A=severe disease,B=moderate disease,C=mild stable disease,D=inactive,but previously active,E=inactive&never affected.BILAG evaluated by scoring each of a list of signs and symptoms as:improving (1)same (2)worse (3)new (4)not present(0)not done(ND).Total BILAG score is sum of scores of 9 domains where A=12,B=8,C=1,D=0,E=0.Total score ranges from 0 to 108 with a higher score indicating > lupus activity.Time to first severe flare, where a severe flare is defined as at least 1BILAG A(Severe disease activity)score in any organ system due to items that are new or worse,compared to BILAG evaluation at previous visit,during 52-Week Treatment.The mITT analysis set was used &"number of subjects analyzed"=subjects who were evaluable for this endpoint.'999' indicated that median was not reached as number of subjects with events were low.

End point type	Secondary

End point timeframe:

Baseline up to Week 56

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	16	11	12
Units: Days				
median (full range (min-max))	99 (29.0 to 337.0)	99 (29.0 to 367.0)	99 (29.0 to 225.0)	99 (28.0 to 162.0)

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7034
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	2.4

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.97

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	1.52

Secondary: DBPC: Number of Subjects With Response Based on Systemic Lupus

Erythematosus Responder Index 4 (SRI-4) at Week 52 in Serologically Active Subgroup

End point title	DBPC: Number of Subjects With Response Based on Systemic Lupus Erythematosus Responder Index 4 (SRI-4) at Week 52 in Serologically Active Subgroup

End point description:

SRI-4 response was defined as >= 4-point reduction in SLEDAI-2K total score, no new BILAG A and no more than 1 new BILAG B domain score, no worsening (<10 percent (%)increase) from baseline in PGA and no treatment failure.SLEDAI-2K assessment consists of 24 items with total score of 0(no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity.BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems.For each organ system A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. PGA assess disease activity on a visual analogue scale =from 0(very well) to 100(very poor).The mITT analysis set was used and "number of subjects analyzed" signifies those subjects with positive anti-double-stranded deoxyribonucleic acid (antidsDNA) and/or low complement levels at screening (Serologically active

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	65	60	63
Units: Subjects	28	38	29	34

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	3.15

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	2.13

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5462
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	2.81

Secondary: DBPC: Number of Subjects With Response Based on Systemic Lupus Erythematosus Responder Index 6 (SRI-6) at Week 52 in Serologically Active Subgroup

End point title	DBPC: Number of Subjects With Response Based on Systemic Lupus Erythematosus Responder Index 6 (SRI-6) at Week 52 in Serologically Active Subgroup

End point description:

SRI-6 response was defined as >= 6-point reduction in SLEDAI-2K total score, no new BILAG A and no more than 1 new BILAG B domain score and no worsening (<10 % increase) from baseline in PGA of Disease Activity and treatment failure. SLEDAI-2K assessment consists of 24 items with total score of 0 (no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system :A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. The PGA assess disease activity on a visual analogue scale = from 0(very well) to 100(very poor). The mITT analysis set was used and "number of subjects analyzed" signifies those subjects with positive antidsDNA and/or low complement levels at screening (Serologically active subgroup).

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	65	60	63
Units: Subjects	17	25	23	23

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2434
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	3.54

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2389
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	3.63

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID

Number of subjects included in analysis	122
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1952
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	3.85

Secondary: DBPC: Time to First British Isles Lupus Assessment Group (BILAG) A or 2B Moderate to Severe Flare

End point title	DBPC: Time to First British Isles Lupus Assessment Group (BILAG) A or 2B Moderate to Severe Flare

End point description:

BILAG Index:assessing clinical signs,symptoms,laboratory parameters related to SLE,divided into 9 organ systems.For each organ system based on alphabetic score:A=severe disease,B=moderate disease,C=mild stable disease,D=inactive,but previously active,E=inactive&never affected.BILAG evaluated by scoring each of a list of signs and symptoms as:improving (1)same (2)worse (3)new (4)not present(0)not done(ND).Total BILAG score is sum of scores of 9 domains where A=12,B=8,C=1,D=0,E=0.Total score ranges from 0 to 108 with a higher score indicating > lupus activity.Time to first severe flare, where a severe flare is defined as at least 1BILAG A(Severe disease activity)score in any organ system due to items that are new or worse,compared to BILAG evaluation at previous visit,during 52-Week Treatment.The mITT analysis set was used &"number of subjects analyzed"=subjects who were evaluable for this endpoint.'99' signifies data not available as number of the subjects with events were low.

End point type	Secondary

End point timeframe:

Baseline up to Week 56

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	27	19	19
Units: Days				
median (full range (min-max))	99 (29.0 to 337.0)	99 (27.0 to 365.0)	99 (29.0 to 308.0)	99 (28.0 to 334.0)

Statistical analyses

Statistical analysis title	Placebo and M2951 25mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD

Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0987
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	2.89

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9201
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.85

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5645
Method	Cox proportional hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.2

Secondary: DBPC: Number of Subjects With British Isles Lupus Assessment Group

(BILAG) 2004 Flare-Free Status During the 52-Week Treatment Period

End point title	DBPC: Number of Subjects With British Isles Lupus Assessment Group (BILAG) 2004 Flare-Free Status During the 52-Week Treatment Period

End point description:

A subject has a flare-free status if no flare has been reported during the 52-week treatment period. Subjects who discontinued treatment prior to Week 52, without having a flare are counted as not being flare free at Week 52. A flare was defined as either 1 or more new BILAG-2004 A (severe disease activity) or 2 or more new BILAG-2004 B (moderate disease activity) items compared to the previous visit. BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system based on alphabetic score: A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. The mITT analysis set was used.

End point type	Secondary

End point timeframe:

up to Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	115	116	114
Units: Subjects	41	35	37	33

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3743
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.37

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD

Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6445
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.54

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2634
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.28

Secondary: DBPC: Annualized Flare Rate

End point title	DBPC: Annualized Flare Rate

End point description:

A flare was defined as either 1 or more new BILAG-2004 A (severe disease activity) or 2 or more new BILAG-2004 B (moderate disease activity) items compared to the previous visit. The occurrence of a new flare was checked for each available visit versus the previous available visit up to Week 52. If no new flares occurred, the number of flares was set to 0. Otherwise all flares were counted leading to the maximum number of flares of 13. The annualized flare rate was calculated as the number of flares divided by the flare exposure time in days multiplied with 365.25 (1 year). The flare exposure time is the time up to Week 52 (date of BILAG-2004 assessment at Week 52) or up to the date of last available BILAG 2004 assessment. The mITT analysis set was used.

End point type	Secondary

End point timeframe:

Baseline up to Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	115	116	114
Units: Annualized flare rate ratio				
number (confidence interval 95%)	0.15 (0.06 to 0.39)	0.23 (0.09 to 0.59)	0.13 (0.05 to 0.33)	0.19 (0.07 to 0.51)

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2989 [28]
Method	Negative binomial regression
Parameter estimate	Rate Ratio
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	3.81

Notes:

[28] - Nominal p-value

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7325 [29]
Method	Negative binomial regression
Parameter estimate	Rate Ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	2.19

Notes:

[29] - Nominal p-value

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID

Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.591 [30]
Method	Negative binomial regression
Parameter estimate	Rate Ratio
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	3.22

Notes:

[30] - Nominal p-value

Secondary: DBPC: Number of Subjects With Low Disease Activity Status, Defined by Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) Score of less than or equal (<=) 2 at Week 52

End point title	DBPC: Number of Subjects With Low Disease Activity Status, Defined by Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) Score of less than or equal (<=) 2 at Week 52

End point description:

Low disease activity is defined as SLEDAI-2K score <=2. SLEDAI-2K is an activity index that measures disease activity and records feature of active lupus as present or not present. SLEDAI-2K uses a weighted checklist to assign a numerical score based on the presence or absence of 24 symptoms at the time of assessment or during the previous 30 days. Each symptom present is assigned between 1 and 8 points based on its usual clinical importance, yielding a total score that ranges from 0 points (no symptoms) to 105 points (presence of all defined symptoms). The mITT analysis set was used.

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	115	116	114
Units: Subjects	26	32	39	28

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD

Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3635
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.47

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0329
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	3.56

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7619
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	2.07

Secondary: DBPC: Number of Subjects With Low Disease Activity Status, Defined by

Clinical Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) Score of less than or equal (<=) 2 at Week 52

End point title	DBPC: Number of Subjects With Low Disease Activity Status, Defined by Clinical Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) Score of less than or equal (<=) 2 at Week 52

End point description:

Low disease activity is defined as SLEDAI-2K score <=2. SLEDAI-2K is an activity index that measures disease activity and records feature of active lupus as present or not present. SLEDAI-2K uses a weighted checklist to assign a numerical score based on the presence or absence of 24 symptoms at the time of assessment or during the previous 30 days. Each symptom present is assigned between 1 and 8 points based on its usual clinical importance, yielding a total score that ranges from 0 points (no symptoms) to 105 points (presence of all defined symptoms). Clinical SLEDAI-2K score is equal to the SLEDAI-2K score from electronic case report form (eCRF) excluding the components 'Increased Deoxyribonucleic acid (DNA) Binding' and 'Low Complement'. The mITT analysis set was used.

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	115	116	114
Units: Subjects	42	50	52	41

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2642
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	2.35

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD

Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1489
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	2.57

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9285
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.7

Secondary: DBPC: Change From Baseline in Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) Score at Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point title	DBPC: Change From Baseline in Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) Score at Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point description:

SLEDAI-2K is an activity index that measures disease activity and records feature of active lupus as present or not present. SLEDAI-2K uses a weighted checklist to assign a numerical score based on the presence or absence of 24 symptoms at the time of assessment or during the previous 30 days. Each symptom present is assigned between 1 and 8 points based on its usual clinical importance, yielding a total score that ranges from 0 points (no symptoms) to 105 points (presence of all defined symptoms). The mITT analysis set was used. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	115	115	113
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Week 4: n= 111, 115, 115, 113	-1 (± 1.9)	-1 (± 2.1)	0 (± 1.9)	-1 (± 2.2)
Week 8: n= 111, 111, 112, 109	-2 (± 3.1)	-2 (± 3.2)	-2 (± 3.0)	-2 (± 3.2)
Week 12: n= 109, 106, 109, 104	-3 (± 3.8)	-3 (± 3.3)	-3 (± 3.2)	-3 (± 3.4)
Week 16: n= 104, 102, 107, 98	-4 (± 3.7)	-3 (± 3.4)	-3 (± 3.4)	-3 (± 3.6)
Week 20: n= 101, 99, 103, 96	-4 (± 4.1)	-4 (± 3.8)	-4 (± 3.4)	-4 (± 3.4)
Week 24: n= 98, 95, 101, 94	-4 (± 4.0)	-4 (± 3.7)	-4 (± 3.6)	-3 (± 3.4)
Week 28: n= 93, 94, 99, 89	-4 (± 3.9)	-4 (± 3.6)	-4 (± 3.5)	-4 (± 3.5)
Week 32: n= 92, 91, 97, 88	-4 (± 4.0)	-4 (± 3.5)	-4 (± 3.7)	-4 (± 3.4)
Week 36: n= 91, 90, 95, 113,	-4 (± 4.3)	-5 (± 3.5)	-5 (± 3.6)	-4 (± 3.5)
Week 40; n= 90, 90, 95, 87	-5 (± 4.1)	-5 (± 3.6)	-5 (± 3.8)	-4 (± 3.3)
Week 44: n= 89, 90, 92, 96	-4 (± 4.0)	-5 (± 3.7)	-5 (± 3.9)	-4 (± 3.5)
Week 48: n= 89, 90, 92, 85	-4 (± 4.1)	-5 (± 3.7)	-5 (± 3.8)	-5 (± 3.3)
Week 52: n= 85, 89, 91, 84	-5 (± 4.0)	-5 (± 3.7)	-5 (± 3.7)	-5 (± 3.9)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Change From Baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity (CLASI-A) Score at Week 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point title	DBPC: Change From Baseline in Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity (CLASI-A) Score at Week 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point description:

CLASI is an validated measurement instrument for lupus erythematosus developed for use in clinical studies that consists of separate scores for the activity of the disease (CLASI-A). The CLASI activity score is calculated on the basis of erythema, scale/hyperkeratosis, mucous membrane involvement, acute hair loss and non-scarring alopecia. The CLASI activity score ranges from 0-70, with higher scores indicating more severe skin disease. Severity categories based on the CLASI activity score are as follows: mild (0-9), moderate (10-20), and severe (21-70). The mITT analysis set was used. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 2, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	113	115	113
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Week 2: n=110, 113, 113, 109	-1 (± 1.9)	-1 (± 1.6)	0 (± 1.6)	0 (± 1.2)
Week 4: n= 111, 113, 115, 113	-1 (± 1.9)	-1 (± 3.5)	-1 (± 2.4)	-1 (± 2.2)
Week 8: n=110, 109, 110, 107	-2 (± 2.8)	-1 (± 4.2)	-1 (± 2.3)	-1 (± 2.5)
Week 12: n= 107, 104, 107, 101	-2 (± 2.8)	-2 (± 3.3)	-2 (± 3.2)	-2 (± 2.7)
Week 16: n= 104, 102, 107, 98	-2 (± 3.1)	-2 (± 3.9)	-2 (± 3.3)	-2 (± 2.7)
Week 20: n= 99, 96, 102, 95	-3 (± 3.6)	-3 (± 4.4)	-3 (± 3.4)	-2 (± 2.9)
Week 24: n= 97, 95, 100, 92	-3 (± 3.5)	-3 (± 4.7)	-3 (± 3.6)	-2 (± 2.7)
Week 28: 92, 91, 96, 89	-3 (± 3.7)	-3 (± 4.6)	-3 (± 3.4)	-2 (± 2.7)
Week 32: n= 91, 91, 96, 87	-3 (± 3.5)	-3 (± 4.4)	-3 (± 3.6)	-3 (± 3.2)
Week 36: n= 90, 89, 95, 86	-3 (± 3.5)	-3 (± 4.6)	-3 (± 3.4)	-3 (± 3.6)
Week 40: n= 90, 90, 92, 85	-3 (± 3.0)	-3 (± 4.6)	-3 (± 3.6)	-3 (± 3.8)
Week 44: n= 89, 90, 92, 85	-3 (± 3.2)	-3 (± 4.5)	-3 (± 3.7)	-3 (± 3.8)
Week 48: n= 88, 89, 91, 83	-3 (± 3.2)	-3 (± 4.7)	-3 (± 3.7)	-3 (± 3.9)
Week 52: n= 84, 86, 89, 84	-3 (± 3.6)	-4 (± 4.8)	-3 (± 3.7)	-3 (± 4.0)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Number of Subjects With Response Based on BILAG-Based Composite Lupus Assessment (BICLA) at Week 52

End point title	DBPC: Number of Subjects With Response Based on BILAG-Based Composite Lupus Assessment (BICLA) at Week 52

End point description:

BICLA response defined as subjects meeting following criteria: 1] At least one gradation of improvement in baseline BILAG scores in all body systems with moderate or severe disease activity at entry (example: 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). The mITT analysis set was used. Here, "Number of subjects Analyzed" signifies those subjects who have at least 1 BILAG A or 2 BILAG B grades at Baseline (BICLA Subpopulation).

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	73	76	70
Units: Subjects	30	29	33	24

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9061
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.88

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.52
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.59

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD

Number of subjects included in analysis	152
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6053
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	2.31

Secondary: DBPC: Change From Baseline in British Isles Lupus Assessment Group (BILAG)-2004 Score at Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point title	DBPC: Change From Baseline in British Isles Lupus Assessment Group (BILAG)-2004 Score at Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point description:

BILAG 2004 disease activity Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system based on alphabetic score: A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. BILAG evaluated by scoring each of a list of signs and symptoms as: improving (1); same (2); worse (3); new (4); not present (0); not done (ND). Total BILAG score is sum of scores of 9 domains where A=12, B=8, C=1, D=0, and E=0. Total score ranges from 0 to 108 with a higher score indicating greater lupus activity. The mITT analysis set was used. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time points.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	111	109	109
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Week 4: n= 108, 108, 108, 105	-4 (± 5.8)	-4 (± 6.1)	-3 (± 6.3)	-4 (± 6.2)
Week 8: n= 110, 111, 109, 109	-6 (± 6.0)	-5 (± 7.0)	-6 (± 6.3)	-6 (± 6.1)
Week 12: n= 109, 106, 107, 104	-7 (± 6.7)	-7 (± 6.8)	-6 (± 7.0)	-6 (± 6.2)
Week 16: n= 104, 102, 105, 98	-7 (± 6.9)	-7 (± 7.6)	-6 (± 6.8)	-6 (± 5.9)
Week 20: n= 101, 99, 102, 96	-7 (± 6.8)	-7 (± 7.3)	-7 (± 7.6)	-6 (± 6.2)
Week 24: n= 97, 95, 100, 94	-8 (± 6.9)	-7 (± 6.5)	-8 (± 7.7)	-6 (± 6.3)
Week 28: n= 93, 94, 98, 89	-8 (± 6.7)	-8 (± 6.9)	-8 (± 7.4)	-7 (± 6.2)
Week 32: n= 92, 91, 96, 89	-9 (± 6.7)	-8 (± 7.3)	-8 (± 7.9)	-7 (± 6.0)
Week 36: n= 91, 90, 95, 88	-8 (± 7.1)	-8 (± 7.2)	-8 (± 7.4)	-7 (± 6.7)
Week 40: n= 88, 90, 95, 87	-9 (± 6.8)	-8 (± 6.7)	-9 (± 7.7)	-7 (± 6.6)
Week 44: n= 88, 90, 92, 85	-9 (± 7.2)	-9 (± 7.2)	-9 (± 7.9)	-7 (± 6.7)

Week 48: n= 89, 90, 92, 85	-8 (± 7.1)	-8 (± 7.2)	-9 (± 7.6)	-7 (± 6.5)
Week 52: n=85, 89, 91, 84	-8 (± 7.0)	-9 (± 6.8)	-9 (± 7.8)	-7 (± 6.7)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Change From Baseline in Physician's Global Assessment (PGA) Score at Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point title	DBPC: Change From Baseline in Physician's Global Assessment (PGA) Score at Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point description:

The Physician's Global Assessment of Disease Activity was recorded using the 100 millimeter horizontal Visual Analog Scale (VAS). Physician rated subject's disease activity on a scale ranged from 0-100 millimeter (mm), where 0 indicated no disease activity and 100 represented maximum disease activity. The mITT analysis set was used. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	111	115	115	113
Units: Millimeter				
arithmetic mean (standard deviation)				
Week 4: n= 111, 115, 115, 113	-8 (± 11.7)	-8 (± 14.1)	-9 (± 13.4)	-9 (± 12.1)
Week 8: n= 110, 109, 111, 107	-13 (± 16.2)	-14 (± 16.5)	-13 (± 15.5)	-14 (± 15.9)
Week 12: n= 107, 104, 107, 101	-18 (± 17.4)	-18 (± 18.8)	-19 (± 18.3)	-18 (± 16.9)
Week 16: n= 104, 102, 105, 98	-21 (± 17.6)	-20 (± 19.7)	-21 (± 18.7)	-19 (± 18.0)
Week 20: n= 99, 96, 102, 95	-23 (± 19.2)	-21 (± 19.5)	-24 (± 17.9)	-20 (± 18.6)
Week 24: n= 97, 95, 100, 92	-24 (± 17.8)	-24 (± 20.0)	-25 (± 19.2)	-21 (± 18.0)
Week 28: n= 92, 91, 96, 89	-26 (± 17.6)	-26 (± 20.3)	-26 (± 18.6)	-24 (± 17.8)
Week 32: n= 91, 91, 96, 87	-26 (± 17.8)	-26 (± 20.8)	-26 (± 19.0)	-26 (± 17.5)
Week 36: n= 90, 89, 95, 86	-26 (± 17.9)	-26 (± 20.9)	-29 (± 18.3)	-26 (± 18.3)
Week 40: n= 90, 90, 91, 85	-27 (± 16.9)	-27 (± 19.1)	-30 (± 19.7)	-25 (± 18.1)
Week 44: n= 89, 90, 92, 85	-28 (± 16.6)	-28 (± 20.1)	-30 (± 20.7)	-26 (± 16.6)
Week 48: n= 88, 89, 91, 83	-29 (± 16.5)	-29 (± 19.5)	-32 (± 18.8)	-28 (± 18.3)
Week 52: n= 84, 86, 89, 84	-29 (± 16.2)	-31 (± 20.7)	-33 (± 19.2)	-27 (± 18.1)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Change From Baseline in Study 36-Item Short Form Health Survey version 2 (SF-36v2) Physical Component Summary Score and Mental Component Summary Scores at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point title	DBPC: Change From Baseline in Study 36-Item Short Form Health Survey version 2 (SF-36v2) Physical Component Summary Score and Mental Component Summary Scores at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point description:

36-Item SF-36 was standardized survey evaluating 8 aspects of functional health and well-being. 8 subscales were relating to either physical or mental health. Physical component summary (PCS) was based primarily on physical functioning, role-physical, bodily pain, and general health scales and mental component summary (MCS) encompasses vitality, social functioning, role-emotional, and mental health scales. Score from mental health, role emotional, social functioning, and vitality domains were averaged to calculate MCS. Total score range for MCS was 0 - 100 (100 = highest level of mental functioning). Score from physical function, role physical, bodily pain, and general health domains were averaged to calculate PCS. Total score range for PCS was 0-100 (100 = highest level of physical functioning). QOL set was used. "Number of subjects analyzed" signifies those subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for the specified category.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 24, 32, 40 and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	114	112	113
Units: Units on a Scale				
arithmetic mean (standard deviation)				
PCS at Week 4 (n=110, 114, 112, 113)	1.2 (± 5.42)	2.5 (± 7.40)	3.5 (± 6.01)	2.2 (± 5.86)
PCS at Week 8 (n=107, 108, 109, 106)	1.8 (± 6.35)	3.5 (± 7.69)	3.0 (± 6.61)	2.2 (± 6.63)
PCS at Week 12 (n=106,102, 103, 101)	2.4 (± 6.44)	3.7 (± 7.71)	4.2 (± 6.68)	3.0 (± 6.99)
PCS at Week 16 (n=101,101, 105, 96)	3.3 (± 7.04)	4.0 (± 7.56)	4.4 (± 5.81)	3.4 (± 6.77)
PCS at Week 24 (n=96, 95,99, 95)	3.4 (± 7.08)	4.6 (± 7.57)	5.4 (± 7.63)	2.8 (± 7.15)
PCS at Week 32 (n=90, 91,93, 88)	3.5 (± 8.03)	3.8 (± 7.36)	5.4 (± 7.24)	3.8 (± 6.89)
PCS at Week 40 (n=88, 89,91, 86)	4.2 (± 7.11)	4.6 (± 7.97)	5.7 (± 7.76)	4.1 (± 8.59)
PCS at Week 52 (n=86, 84,87, 82)	3.7 (± 8.32)	5.4 (± 7.05)	6.5 (± 8.58)	4.8 (± 7.76)
MCS at Week 4 (n= 110, 114, 112, 113)	3.9 (± 9.38)	1.7 (± 9.25)	1.9 (± 7.92)	2.4 (± 7.68)
MCS at Week 8 (n= 107, 108, 109, 106)	2.5 (± 8.59)	2.2 (± 8.81)	1.6 (± 8.48)	3.6 (± 9.04)
MCS at Week 12 (n= 106,102,103, 101)	3.1 (± 10.07)	3.1 (± 8.45)	0.8 (± 10.39)	2.9 (± 8.89)
MCS at Week 16 (n= 101,101,105, 96)	3.6 (± 9.84)	2.5 (± 8.39)	2.8 (± 9.39)	2.9 (± 9.13)
MCS at Week 24 (n= 96,95,99, 95)	2.9 (± 9.75)	2.4 (± 8.41)	3.4 (± 9.68)	2.7 (± 8.87)
MCS at Week 32 (n= 90,91,93, 88)	3.5 (± 8.55)	1.8 (± 9.51)	2.8 (± 9.71)	4.3 (± 9.03)
MCS at Week 40 (n= 88, 89, 91, 86)	4.5 (± 8.81)	1.5 (± 10.55)	3.2 (± 9.81)	4.0 (± 9.85)
MCS at Week 52 (n= 86, 84, 87, 82)	3.8 (± 9.45)	1.7 (± 9.91)	3.9 (± 11.21)	4.6 (± 9.80)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Change From Baseline in European Quality of Life 5-dimensions (EQ-5D-5L) Health Outcome Questionnaire at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point title	DBPC: Change From Baseline in European Quality of Life 5-dimensions (EQ-5D-5L) Health Outcome Questionnaire at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point description:

The EQ-5D-5L questionnaire is a generic measure of health status that provides a simple descriptive profile and a single index value. The EQ-5D-5L profile defines health in terms of mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each dimension has five levels: 1: no problems, 2: slight problems, 3: moderate problems, 4: severe problems, and 5: extreme problems. Responses were used to generate a weighted summary index (EQ-5D index), which ranges from 0 (dead) to 1.00 (perfect health). A higher score indicates better health and positive changes from baseline indicate improvement of health. Quality of Life analysis set was used. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 24, 32, 40, and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	114	112	113
Units: Units on a Scale				
arithmetic mean (standard deviation)				
Week 4: n= 110, 114, 112, 113	0.036 (± 0.1626)	0.045 (± 0.1931)	0.036 (± 0.1618)	0.038 (± 0.1908)
Week 8: n= 107, 108, 109, 106	0.034 (± 0.2164)	0.064 (± 0.2505)	0.046 (± 0.1842)	0.061 (± 0.1603)
Week 12: n= 106, 102, 103, 101	0.061 (± 0.2014)	0.070 (± 0.2189)	0.055 (± 0.1912)	0.065 (± 0.1732)
Week 16: n= 101, 101, 105, 96	0.083 (± 0.1818)	0.072 (± 0.2252)	0.067 (± 0.2287)	0.056 (± 0.1738)
Week 24: n= 96, 95, 99, 95	0.080 (± 0.1901)	0.067 (± 0.2271)	0.086 (± 0.2110)	0.055 (± 0.1817)
Week 32: n= 90, 91, 93, 88	0.083 (± 0.1758)	0.067 (± 0.2262)	0.075 (± 0.2009)	0.071 (± 0.1941)
Week 40: n= 88, 89, 91, 86	0.093 (± 0.1521)	0.061 (± 0.1850)	0.090 (± 0.1853)	0.084 (± 0.2172)
Week 52: n= 86, 84, 87, 82	0.096 (± 0.2092)	0.078 (± 0.2197)	0.102 (± 0.2224)	0.096 (± 0.2051)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Change From Baseline in European Quality of Life 5-dimensions (EQ-5D-5L) Visual Analog Scale (VAS) at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point title	DBPC: Change From Baseline in European Quality of Life 5-dimensions (EQ-5D-5L) Visual Analog Scale (VAS) at Week 4,

	8, 12, 16, 24, 32, 40 and 52

End point description:

The EQ-5D-5L questionnaire is a generic measure of health status that provides a simple descriptive profile and a single index value. The EQ-5D-5L profile defines health in terms of mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each dimension has five levels: 1: no problems, 2: slight problems, 3: moderate problems, 4: severe problems, and 5: extreme problems. The responses were used to derive overall score using a visual analog scale (VAS) that ranged from 0 to 100 millimeter (mm), where 0 was the worst health you can imagine and 100 was the best health you can imagine. Quality of Life analysis set was used. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 24, 32, 40, and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	114	112	113
Units: Millimeter				
arithmetic mean (standard deviation)				
Week 4: n= 110, 114, 112, 113	3 (± 16.8)	2 (± 19.0)	4 (± 17.6)	4 (± 18.2)
Week 8: n= 107, 108, 109, 106	3 (± 18.8)	6 (± 20.0)	4 (± 14.5)	6 (± 16.5)
Week 12: n= 106, 102, 103, 101	5 (± 19.7)	6 (± 17.4)	5 (± 17.2)	4 (± 16.8)
Week 16: n= 101, 101, 105, 96	7 (± 19.3)	5 (± 18.1)	6 (± 18.5)	4 (± 15.5)
Week 24: n= 96, 95, 99, 95	7 (± 18.7)	5 (± 18.4)	9 (± 20.4)	4 (± 17.3)
Week 32: n= 90, 91, 93, 88	8 (± 17.2)	4 (± 21.1)	7 (± 17.8)	7 (± 16.6)
Week 40: n= 88, 89, 91, 86	8 (± 18.1)	6 (± 18.1)	10 (± 19.5)	8 (± 18.9)
Week 52: n= 86, 84, 87, 82	8 (± 19.9)	8 (± 18.6)	10 (± 21.3)	10 (± 18.9)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Change From Baseline in Lupus Quality of Life (LupusQoL) Questionnaire Score at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point title	DBPC: Change From Baseline in Lupus Quality of Life (LupusQoL) Questionnaire Score at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point description:

The Lupus QoL assessment is a 34 item questionnaire across 8 domains that is designed to find out how SLE affects a subject's life. Domains include physical health (PH), pain, planning, intimate relationships (IR), burden to others (BTO), emotional health (EH), body image, and fatigue. Subjects indicate their responses on a 5-point Likert response format, where 4=never,3=occasionally,2= a good bit of the time,1=most of the time and 0=worst of the time. Summary scores can be calculated for all 8 domains. LupusQoL score for each domain was reported on a 0 to 100 scale, with greater values indicating better health related QoL. QOL analysis set was used. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 24, 32, 40, and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	114	112	113
Units: Units on a scale				
arithmetic mean (standard deviation)				
PH Week 4: n=110,114,112,113	1.9 (± 12.58)	4.7 (± 17.68)	4.0 (± 14.04)	3.5 (± 13.43)
PH Week 8: n=107, 108, 109, 106	2.8 (± 15.20)	6.3 (± 19.94)	3.8 (± 17.64)	4.6 (± 14.69)
PH Week 12: n= 106, 102, 103, 101	4.8 (± 16.75)	6.7 (± 19.78)	5.6 (± 15.95)	5.7 (± 14.94)
PH Week 16: n= 101, 101, 105, 96	6.6 (± 17.45)	6.1 (± 18.71)	7.4 (± 17.61)	6.2 (± 15.59)
PH Week 24: n= 96, 95, 99, 95	6.9 (± 17.17)	7.2 (± 18.59)	8.4 (± 20.47)	6.1 (± 13.63)
PH Week 32: n= 90, 91, 93, 88	5.7 (± 16.82)	6.7 (± 19.45)	9.4 (± 17.21)	7.0 (± 16.21)
PH Week 40: n= 88, 89, 91, 86	7.6 (± 15.32)	8.2 (± 17.38)	9.6 (± 19.10)	7.1 (± 17.98)
PH Week 52: n= 86, 84, 87, 82	7.1 (± 20.39)	9.0 (± 18.44)	11.6 (± 19.88)	7.9 (± 18.73)
Pain Week 4: n= 110, 114, 112, 113	3.6 (± 16.30)	6.7 (± 21.81)	9.0 (± 20.90)	5.7 (± 16.26)
Pain Week 8: n=107, 108, 109, 106	4.8 (± 18.71)	9.9 (± 24.65)	7.3 (± 21.76)	6.7 (± 18.31)
Pain Week 12: n= 106, 102, 103, 101	7.5 (± 19.04)	8.8 (± 24.00)	9.8 (± 23.35)	5.5 (± 14.73)
Pain Week 16: n= 101, 101, 105, 96	9.4 (± 18.58)	8.3 (± 25.60)	10.5 (± 26.33)	6.9 (± 15.47)
Pain Week 24: n= 96, 95, 99, 95	9.4 (± 19.95)	9.3 (± 24.31)	13.0 (± 28.18)	6.2 (± 17.02)
Pain Week 32: n= 90, 91, 93, 88	6.7 (± 23.74)	9.2 (± 24.60)	12.8 (± 22.87)	8.7 (± 17.18)
Pain Week 40: n= 88, 89, 91, 86	11.0 (± 19.43)	10.9 (± 23.68)	15.3 (± 23.81)	9.6 (± 20.51)
Pain Week 52: n= 86, 84, 87, 82	10.2 (± 21.37)	12.9 (± 22.64)	14.9 (± 26.11)	9.6 (± 19.99)
Planning Week 4: n=110,114, 112, 113	4.8 (± 20.14)	4.9 (± 19.64)	5.4 (± 24.30)	4.6 (± 18.73)
Planning Week 8: n= 107, 108, 109, 106	5.5 (± 23.32)	8.4 (± 23.25)	5.8 (± 25.14)	3.9 (± 22.98)
Planning Week 12: n= 106,102,103,101	7.8 (± 23.58)	5.8 (± 23.39)	6.8 (± 25.74)	5.1 (± 20.55)
Planning Week 16: n=101,101,105,96	8.3 (± 21.65)	5.3 (± 24.12)	6.5 (± 28.00)	6.3 (± 22.91)
Planning Week 24: n= 96,95, 99, 95	7.9 (± 22.92)	8.1 (± 23.55)	11.5 (± 29.08)	5.6 (± 21.79)
Planning Week 32: n= 90,91,93,88	6.5 (± 24.82)	7.6 (± 22.66)	9.9 (± 25.90)	6.9 (± 22.07)
Planning Week 40: n= 88,89,91,86	9.0 (± 20.69)	7.8 (± 23.19)	11.6 (± 26.17)	8.0 (± 23.52)
Planning Week 52: n= 86,84,87,82	9.9 (± 22.38)	7.0 (± 23.12)	9.9 (± 28.29)	10.5 (± 21.59)
IR Week 4: n= 74,88,80,71	3.4 (± 26.11)	1.6 (± 28.29)	4.7 (± 24.06)	3.2 (± 24.06)
IR Week 8: n= 70,81,75,61	8.2 (± 30.31)	4.2 (± 28.44)	9.7 (± 29.10)	3.7 (± 18.73)
IR Week 12: n= 70,75,65,59	5.5 (± 27.31)	4.7 (± 25.65)	2.3 (± 30.37)	6.4 (± 21.32)
IR Week 16: n= 60,72,69,53	8.8 (± 26.77)	1.6 (± 30.76)	3.8 (± 32.46)	4.2 (± 22.99)
IR Week 24: n= 59,70,62,47	6.4 (± 30.12)	2.1 (± 28.79)	6.7 (± 30.76)	5.3 (± 26.29)
IR Week 32: n= 54,66,54,52	2.5 (± 28.77)	1.3 (± 31.78)	6.5 (± 29.41)	1.4 (± 27.86)
IR Week 40: n= 49,61,55,48	12.0 (± 27.59)	6.6 (± 27.91)	6.4 (± 32.53)	7.8 (± 22.72)
IR Week 52: n= 51,60,49,45	7.4 (± 26.48)	4.4 (± 28.36)	8.4 (± 29.58)	8.9 (± 24.52)
BTO Week 4: n= 110,114,112,113	5.8 (± 23.83)	5.2 (± 22.84)	6.8 (± 24.85)	2.2 (± 24.24)
BTO Week 8: n= 107,108,109,106	5.6 (± 22.42)	9.3 (± 27.17)	5.7 (± 25.80)	8.0 (± 25.79)
BTO Week 12: n= 106,102,103,101	8.6 (± 25.86)	6.7 (± 28.00)	7.4 (± 25.93)	7.3 (± 24.74)
BTO Week 16: n= 101,101,105,96	11.8 (± 26.17)	8.1 (± 23.32)	6.7 (± 25.80)	7.4 (± 24.30)
BTO Week 24: n= 96, 95, 99,95	10.3 (± 28.68)	9.0 (± 24.12)	11.8 (± 27.15)	5.8 (± 26.21)
BTO Week 32: n= 90,91,93,88	10.6 (± 29.42)	6.8 (± 24.09)	9.6 (± 27.14)	8.4 (± 28.21)
BTO Week 40: n= 88,89,91,86	16.1 (± 25.07)	12.4 (± 21.91)	12.4 (± 28.74)	12.1 (± 25.78)
BTO Week 52: n= 86,84,87,82	15.3 (± 26.96)	10.7 (± 22.13)	13.0 (± 30.04)	10.5 (± 25.89)
EH Week 4: n= 110,114,112,113	6.4 (± 15.37)	4.7 (± 18.48)	4.2 (± 18.45)	1.8 (± 16.73)
EH Week 8: n= 107,108,109,106	4.5 (± 15.15)	7.0 (± 19.26)	2.3 (± 19.51)	5.3 (± 15.53)

EH Week 12: n= 106,102,103,101	6.3 (± 17.23)	7.6 (± 21.08)	4.9 (± 20.99)	4.7 (± 16.39)
EH Week 16: n= 101,101,105,96	8.3 (± 15.86)	7.5 (± 19.59)	7.4 (± 18.56)	6.2 (± 18.32)
EH Week 24: n= 96,95,99,95	7.1 (± 17.31)	5.6 (± 24.02)	8.9 (± 20.97)	4.3 (± 20.04)
EH Week 32: n= 90,91,93,88	6.3 (± 17.07)	4.3 (± 23.55)	9.0 (± 22.66)	6.0 (± 20.56)
EH Week 40: n= 88,89,91,86	8.4 (± 16.08)	8.3 (± 19.94)	7.6 (± 21.52)	6.7 (± 19.14)
EH Week 52: n= 86,84,87,82	8.5 (± 17.43)	6.4 (± 21.31)	8.2 (± 22.77)	7.6 (± 18.80)
Body Image Week 4:n=96,97,92,93	3.1 (± 17.70)	8.4 (± 24.41)	2.5 (± 24.60)	4.0 (± 18.79)
Body Image Week 8:n=90,92,91,85	5.7 (± 18.37)	7.5 (± 23.40)	-1.3 (± 27.06)	6.5 (± 17.30)
Body Image Week 12:n=88,84,83,85	6.5 (± 18.57)	7.1 (± 21.07)	2.3 (± 26.86)	6.6 (± 16.53)
Body Image Week 16:n=84,82,85,81	6.7 (± 18.10)	7.6 (± 23.11)	-0.4 (± 25.31)	5.7 (± 20.39)
Body Image Week 24:n=75,79,75,77	6.7 (± 20.84)	10.2 (± 20.47)	5.8 (± 27.31)	6.7 (± 21.80)
Body Image Week 32:n=71,76,68,73	5.1 (± 20.08)	8.1 (± 23.71)	3.3 (± 24.99)	5.8 (± 21.54)
Body Image Week 40:n=71,76,66,72	7.7 (± 14.11)	8.2 (± 23.99)	4.6 (± 26.67)	9.0 (± 18.31)
Body Image Week 52:n=74,68,66,67	6.6 (± 16.92)	9.8 (± 21.46)	5.1 (± 27.30)	7.8 (± 21.56)
Fatigue Week 4:n=110,114,112,113	4.4 (± 16.71)	4.3 (± 18.98)	6.2 (± 19.91)	3.9 (± 17.08)
Fatigue Week 8:n=107,108,109,106	5.0 (± 19.22)	7.1 (± 21.31)	4.9 (± 20.61)	4.5 (± 16.78)
Fatigue Week 12:n= 106,102,103,101	6.7 (± 18.22)	5.8 (± 21.30)	7.3 (± 23.11)	5.0 (± 16.08)
Fatigue Week 16:n=101,101,105,96	7.7 (± 17.61)	6.6 (± 21.39)	7.1 (± 24.16)	4.1 (± 15.81)
Fatigue Week 24: n=96,95,99,95	7.5 (± 19.06)	4.8 (± 23.34)	9.0 (± 26.00)	3.6 (± 14.20)
Fatigue Week 32: n=90,91,93,88	7.0 (± 19.20)	3.7 (± 22.71)	8.5 (± 22.96)	4.1 (± 17.24)
Fatigue Week 40: n= 88,89,91,86	11.3 (± 20.03)	6.1 (± 25.28)	11.0 (± 25.18)	5.3 (± 16.73)
Fatigue Week 52: n= 86,84,87,82	8.9 (± 21.15)	4.5 (± 24.78)	11.2 (± 22.56)	6.7 (± 17.89)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Number of Subjects With Patient Global Impression of Change (PGIC) Scale Score of Any Improvement, no Change and Any Worsening

End point title	DBPC: Number of Subjects With Patient Global Impression of Change (PGIC) Scale Score of Any Improvement, no Change and Any Worsening

End point description:

The PGIC is a self-rated scale that asks the subject to describe the change in activity limitations, symptoms, emotions, and overall quality of life (QoL) related to the subjects painful condition on the following scale: 1 (very much improved), 2 (much improved), 3 (minimally improved), 4 (no change), 5 (minimally worse), 6 (much worse) and 7 (very much worse). Number of subjects in the PGIC categories of any improvement (that is PGIC scale score 1, 2 or 3), no change (that is PGIC scale score 4) and any worsening (that is PGIC scale score 5, 6 or 7) are reported. QOL analysis set was used. Here, "n" signifies those subjects who were evaluable for specified category at given time points.

End point type	Secondary

End point timeframe:

Week 4, 8, 12, 16, 24, 32, 40, and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	114	113	113
Units: Subjects				
Week 4 Any Improvement: n= 112, 114, 113, 113	69	78	81	71
Week 8 Any Improvement: n= 110, 110, 110, 109	80	81	85	75
Week 12 Any Improvement: n= 108, 105,107,104	78	82	81	77
Week 16 Any Improvement: n= 104, 101,105,98	75	81	87	79
Week 24 Any Improvement: n= 98, 95, 101, 95	67	77	87	73
Week 32 Any Improvement: n= 91, 91, 95, 89	70	70	80	72
Week 40 Any Improvement: n= 89, 89, 93, 87	67	69	80	73
Week 52 Any Improvement: n= 88, 89, 90, 85	66	64	76	64
Week 4 No Change: n= 112, 114, 113, 113	33	27	23	34
Week 8 No Change: n= 110, 110, 110,109	22	18	19	28
Week 12 No Change: n= 108, 105, 107, 104	23	13	15	20
Week 16 No Change: n= 104, 101,105,98	23	13	16	15
Week 24 No Change: n= 98, 95, 101, 95	23	12	7	17
Week 32 No Change: n= 91, 91, 95, 89	16	15	8	13
Week 40 No Change: n= 89, 89, 93, 87	19	12	7	9
Week 52 No Change: n= 88, 89, 90, 85	14	18	6	13
Week 4 Any Worsening: n= 112, 114, 113, 113	8	9	8	8
Week 8 Any Worsening: n= 110, 110, 110, 109	5	9	5	3
Week 12 Any Worsening: n= 108, 105, 107, 104	5	7	7	4
Week 16 Any Worsening: n= 104, 101, 105, 98	3	7	2	2
Week 24 Any Worsening: n= 98, 95, 101, 95	6	6	5	5
Week 32 Any Worsening: n= 91, 91, 95, 89	4	6	5	3
Week 40 Any Worsening: n= 89, 89, 93, 87	2	8	4	4
Week 52 Any Worsening: n= 88, 89, 90, 85	6	1	5	4
Week 4 Missing: n=112, 114, 113, 113	2	0	1	0
Week 8 Missing: n= 110, 110, 110, 109	3	2	1	3
Week 12 Missing: n= 108, 105, 107, 104	2	3	4	3
Week 16 Missing: n= 104, 101, 105, 98	3	0	0	2
Week 24 Missing: n= 98, 95, 101, 95	2	0	2	0
Week 32 Missing: n= 91, 91, 95, 89	1	0	2	1
Week 40 Missing: n= 89, 89, 93, 87	1	0	2	1
Week 52 Missing: n= 88, 89, 90, 85	2	6	3	4

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point title	DBPC: Change From Baseline in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) Score at Week 4, 8, 12, 16, 24, 32, 40 and 52

End point description:

The FACIT-Fatigue score was calculated according to a 13-item questionnaire that assess self reported fatigue and its impact upon daily activities and function. It uses a 5-point Likert-type scale (0 = not at all; 1 = a little bit; 2 = somewhat; 3 = quite a bit; 4 = very much). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse possible score) to 52 (best score). A higher score reflected an improvement in the subjects's health status. Quality of Life analysis set was used. "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 4, 8, 12, 16, 24, 32, 40, and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	110	114	112	113
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 4: n= 110, 114, 112, 113	3 (± 8.0)	2 (± 7.8)	4 (± 9.1)	3 (± 7.7)
Week 8: n= 107, 108, 109, 106	3 (± 8.7)	3 (± 8.3)	3 (± 9.1)	5 (± 8.2)
Week 12: n= 106, 102, 103, 101	3 (± 10.0)	4 (± 9.7)	3 (± 9.7)	4 (± 8.1)
Week 16: n= 101, 101, 105, 96	4 (± 9.8)	3 (± 9.8)	4 (± 10.2)	3 (± 8.4)
Week 24: n= 96, 95, 99, 95	3 (± 9.9)	4 (± 8.5)	5 (± 10.3)	3 (± 7.5)
Week 32: n= 90, 91, 93, 88	4 (± 9.6)	4 (± 9.5)	5 (± 9.7)	4 (± 6.8)
Week 40: n= 88, 89, 91, 86	4 (± 8.8)	3 (± 8.6)	6 (± 9.9)	4 (± 8.5)
Week 52: n= 86, 84, 87, 82	4 (± 9.9)	4 (± 7.9)	5 (± 9.7)	5 (± 8.7)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Number of Subjects With Change From Baseline in Prednisone Equivalent Corticosteroid (CS) dose by >=25% to a dose of <=7.5 Milligram per day

(mg/day), With no BILAG A or 2B Flare in Disease Activity at Week 52	
End point title	DBPC: Number of Subjects With Change From Baseline in Prednisone Equivalent Corticosteroid (CS) dose by >=25% to a dose of <=7.5 Milligram per day (mg/day), With no BILAG A or 2B Flare in Disease Activity at Week 52

End point description:

BILAG A or 2B flare is defined as at least 1 BILAG A grade or 2 BILAG B grade in any organ system due to items that are new or worse, compared to the BILAG evaluation at the previous visit, during the 52 week treatment period. BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system based on alphabetic score: A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. The mITT analysis set was used. Here, "number of subjects analyzed" signifies those subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline and Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	68	70	71
Units: Subjects	19	23	20	21

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Rate difference
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	21.2

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD

Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Rate Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.5
upper limit	15.6

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Rate difference
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.5
upper limit	16.6

Secondary: DBPC: Change From Baseline to Week 52 in Prednisone Equivalent Corticosteroid (CS) Daily Dose at at Week 1, 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point title	DBPC: Change From Baseline to Week 52 in Prednisone Equivalent Corticosteroid (CS) Daily Dose at at Week 1, 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point description:

Change From Baseline in Prednisone-equivalent CS Daily Dose at Week 1, 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52 were reported. The mITT analysis set included all randomized subjects who had received at least one dose of IMP (Evobrutinib or placebo) and have at least one Baseline and one post Baseline disease assessment among the following: SFI, SLEDAI 2K, PGA, BILAG 2004, CLASI. Here, "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint and "n" signifies those subjects who were evaluable for specified category at given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	113	113	116	114
Units: Milligram (mg)				
arithmetic mean (standard deviation)				
Week 1: n= 48, 58, 60, 52	0.21 (± 1.443)	0.00 (± 0.000)	0.00 (± 0.000)	0.00 (± 0.000)
Week 2: n= 113, 113, 116, 114	0.10 (± 1.206)	-0.07 (± 0.524)	0.00 (± 0.000)	-0.13 (± 1.405)
Week 4: n= 111, 113, 115, 111	0.01 (± 1.267)	-0.45 (± 2.879)	-0.04 (± 0.739)	-0.15 (± 1.428)
Week 6: n= 57, 47, 55, 55	-1.07 (± 3.563)	-0.64 (± 3.275)	-0.59 (± 2.095)	-0.70 (± 3.484)
Week 8: n= 108, 110, 110, 105	-0.57 (± 2.588)	-1.24 (± 3.915)	-1.09 (± 3.640)	-1.02 (± 3.422)
Week 10: n= 55, 49, 61, 55	-1.43 (± 3.985)	-2.04 (± 5.146)	-1.56 (± 4.137)	-2.50 (± 4.971)
Week 12: n= 107, 102, 107, 99	-1.26 (± 3.260)	-1.85 (± 4.158)	-1.73 (± 4.574)	-1.97 (± 4.150)
Week 14: n= 60, 51, 63, 57	-2.00 (± 4.569)	-2.70 (± 5.428)	-1.87 (± 4.489)	-2.76 (± 5.125)
Week 16: n= 102, 101, 104, 97	-1.67 (± 4.427)	-2.70 (± 4.955)	-2.47 (± 5.365)	-2.40 (± 4.535)
Week 20: n= 98, 94, 101, 94	-1.94 (± 4.054)	-2.82 (± 4.905)	-2.64 (± 5.489)	-2.53 (± 4.727)
Week 24: n= 93, 95, 99, 91	-1.99 (± 4.228)	-2.64 (± 5.066)	-2.61 (± 5.568)	-2.34 (± 5.330)
Week 28: n= 92, 91, 97, 89	-2.23 (± 4.439)	-2.97 (± 4.981)	-3.07 (± 6.068)	-2.46 (± 5.371)
Week 32: n= 92, 90, 95, 88	-2.45 (± 4.584)	-3.13 (± 5.193)	-3.18 (± 6.161)	-2.44 (± 5.347)
Week 36: n= 90, 90, 95, 87	-2.42 (± 4.835)	-3.31 (± 5.327)	-3.18 (± 6.136)	-2.37 (± 5.445)
Week 40: n= 90, 90, 92, 86	-2.08 (± 6.149)	-3.21 (± 5.280)	-3.24 (± 6.218)	-2.67 (± 5.202)
Week 44: n= 89, 90, 92, 85	-2.42 (± 4.833)	-3.21 (± 5.280)	-3.27 (± 6.254)	-2.56 (± 5.121)
Week 48: n= 86, 89, 91, 84	-2.38 (± 4.895)	-3.22 (± 5.310)	-3.37 (± 6.265)	-2.62 (± 5.136)
Week 52: n= 99, 100, 100, 96	-1.70 (± 5.470)	-2.94 (± 5.534)	-3.09 (± 5.981)	-2.63 (± 5.673)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Number of Subjects With Reduction From Baseline in Prednisone Equivalent Corticosteroid (CS) Daily Dose by > 0 to 25%, >25% to 50%, >50% to 100% or an Increase at Week 1, 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point title	DBPC: Number of Subjects With Reduction From Baseline in Prednisone Equivalent Corticosteroid (CS) Daily Dose by > 0 to 25%, >25% to 50%, >50% to 100% or an Increase at Week 1, 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52

End point description:

Number of Subjects With Reduction From Baseline in Prednisone-equivalent Corticosteroid (CS) Daily

Dose by > 0 to 25%, >25% to 50%, >50% to 100% or an Increase at Week 1, 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52 were reported. The mITT analysis set included all randomized subjects who had received at least one dose of IMP (Evobrutinib or placebo) and have at least one Baseline and one post Baseline disease assessment among the following: SFI, SLEDAI 2K, PGA, BILAG 2004, CLASI.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 2, 4, 6, 8, 10, 12, 14, 16, 20, 24, 28, 32, 36, 40, 44, 48, and 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	115	116	114
Units: Subjects				
Reduction of dose by >0-25% Week 1	0	0	0	0
Reduction of dose by >0-25% Week 2	1	2	0	0
Reduction of dose by >0-25% Week 4	1	5	2	1
Reduction of dose by >0-25% Week 6	3	4	3	4
Reduction of dose by >0-25% Week 8	6	6	5	6
Reduction of dose by >0-25% Week 10	0	3	4	5
Reduction of dose by >0-25% Week 12	5	11	8	6
Reduction of dose by >0-25% Week 14	2	2	4	5
Reduction of dose by >0-25% Week 16	5	10	5	6
Reduction of dose by >0-25% Week 20	5	10	5	5
Reduction of dose by >0-25% Week 24	4	10	5	5
Reduction of dose by >0-25% Week 28	2	8	5	4
Reduction of dose by >0-25% Week 32	1	7	4	3
Reduction of dose by >0-25% Week 36	1	5	4	3
Reduction of dose by >0-25% Week 40	1	5	3	3
Reduction of dose by >0-25% Week 44	1	5	3	3
Reduction of dose by >0-25% Week 48	0	5	4	3
Reduction of dose by >0-25% Week 52	1	5	4	4
Reduction of dose by >25- 50% Week 1	0	0	0	0
Reduction of dose by >25- 50% Week 2	0	0	0	0
Reduction of dose by >25- 50% Week 4	1	2	1	0
Reduction of dose by >25- 50% Week 6	4	1	2	0
Reduction of dose by >25- 50% Week 8	5	9	6	5
Reduction of dose by >25- 50% Week 10	7	6	4	10
Reduction of dose by >25- 50% Week 12	14	9	10	15
Reduction of dose by >25- 50% Week 14	7	6	2	8
Reduction of dose by >25- 50% Week 16	16	12	9	16
Reduction of dose by >25- 50% Week 20	13	11	8	14
Reduction of dose by >25- 50% Week 24	12	9	8	13
Reduction of dose by >25- 50% Week 28	14	12	9	16
Reduction of dose by >25- 50% Week 32	15	11	8	16

Reduction of dose by >25- 50% Week 36	15	13	6	15
Reduction of dose by >25- 50% Week 40	15	15	6	16
Reduction of dose by >25- 50% Week 44	15	15	6	16
Reduction of dose by >25- 50% Week 48	15	14	6	17
Reduction of dose by >25- 50% Week 52	16	12	7	17
Reduction of dose by >50-100% Week 1	0	0	0	0
Reduction of dose by >50-100% Week 2	0	0	0	1
Reduction of dose by >50-100% Week 4	0	1	0	1
Reduction of dose by >50-100% Week 6	1	1	0	1
Reduction of dose by >50-100% Week 8	1	3	4	3
Reduction of dose by >50-100% Week 10	2	3	3	4
Reduction of dose by >50-100% Week 12	1	6	6	6
Reduction of dose by >50-100% Week 14	5	6	7	7
Reduction of dose by >50-100% Week 16	5	13	13	9
Reduction of dose by >50-100% Week 20	7	13	14	11
Reduction of dose by >50-100% Week 24	7	14	13	11
Reduction of dose by >50-100% Week 28	9	14	15	11
Reduction of dose by >50-100% Week 32	11	16	16	12
Reduction of dose by >50-100% Week 36	10	17	18	11
Reduction of dose by >50-100% Week 40	10	15	18	11
Reduction of dose by >50-100% Week 44	10	15	18	10
Reduction of dose by >50-100% Week 48	9	15	19	10
Reduction of dose by >50-100% Week 52	9	17	19	12
Increased from Baseline Week 1	1	0	0	0
Increased from Baseline Week 2	2	0	0	0
Increased from Baseline Week 4	2	1	1	0
Increased from Baseline Week 6	1	1	0	0
Increased from Baseline Week 8	2	1	1	0
Increased from Baseline Week 10	1	1	0	0
Increased from Baseline Week 12	1	1	1	0
Increased from Baseline Week 14	1	0	0	0
Increased from Baseline Week 16	1	1	1	0
Increased from Baseline Week 20	0	0	0	0
Increased from Baseline Week 24	0	0	0	0
Increased from Baseline Week 28	0	0	0	1
Increased from Baseline Week 32	0	0	0	1
Increased from Baseline Week 36	0	0	0	1
Increased from Baseline Week 40	1	0	0	1
Increased from Baseline Week 44	0	0	0	1
Increased from Baseline Week 48	0	0	0	1

Increased from Baseline Week 52	2	0	0	2

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Cumulative Prednisone Equivalent Corticosteroid (CS) Dose at Week 52

End point title	DBPC: Cumulative Prednisone Equivalent Corticosteroid (CS) Dose at Week 52

End point description:

Cumulative Prednisone-equivalent Corticosteroid (CS) Dose was calculated at Week 52. The mITT analysis set included all randomized subjects who had received at least one dose of IMP (Evobrutinib or placebo) and have at least one Baseline and one post Baseline disease assessment among the following: SFI, SLEDAI 2K, PGA, BILAG 2004, CLASI.

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	115	116	114
Units: Milligrams				
arithmetic mean (standard deviation)	2267.66 (± 1507.652)	2209.46 (± 1922.557)	2137.70 (± 1618.688)	2205.56 (± 1737.092)

Statistical analyses

No statistical analyses for this end point

Secondary: DBPC: Number of Subjects With a Sustained Reduction of Oral Corticosteroids (OCS) Dose to 7.5 mg Prednisone Equivalent per day or Less With Response Based on Systemic Lupus Erythematosus Responder Index 4 (SRI-4) at Week 52

End point title	DBPC: Number of Subjects With a Sustained Reduction of Oral Corticosteroids (OCS) Dose to 7.5 mg Prednisone Equivalent per day or Less With Response Based on Systemic Lupus Erythematosus Responder Index 4 (SRI-4) at Week 52

End point description:

SRI-4 response was defined as >= 4-point reduction in SLEDAI-2K total score, no new BILAG A and no more than 1 new BILAG B domain score, no worsening (<10 % increase) from baseline in PGA of Disease Activity and no treatment failure. SLEDAI-2K assessment consists of 24 items with total score of 0(no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. The PGA assess

disease activity on a visual analogue scale =from 0(very well) to 100(very poor). The mITT analysis set was used. "Number of subjects analyzed" signifies subjects who maintained Sustained Reduction of OCS were evaluable for this endpoint.

End point type	Secondary
End point timeframe:	
Week 52	

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	56	59	63	57
Units: Subjects	43	45	43	41

Statistical analyses

Statistical analysis title	Placebo and M2951 25mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7728
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	2.82

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3314
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	1.54

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	113
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7205
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	2.04

Secondary: DBPC: Number of Subjects With a Sustained Reduction of Oral Corticosteroids (OCS) Dose to 7.5 mg Prednisone Equivalent per day or Less With Response Based on Systemic Lupus Erythematosus Responder Index 6 (SRI-6) at Week 52

End point title	DBPC: Number of Subjects With a Sustained Reduction of Oral Corticosteroids (OCS) Dose to 7.5 mg Prednisone Equivalent per day or Less With Response Based on Systemic Lupus Erythematosus Responder Index 6 (SRI-6) at Week 52

End point description:

SRI-6 response was defined as >= 6-point reduction in SLEDAI-2K total score, no new BILAG A and no more than 1 new BILAG B domain score and no worsening (<10% increase) from baseline in PGA of Disease Activity and treatment failure. SLEDAI-2K assessment consists of 24 items with total score of 0 (no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system :A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. The PGA assess disease activity on a visual analogue scale =from 0(very well) to 100(very poor). The mITT analysis set was used. "Number of subjects analyzed" signifies subjects who achieved SLEDAI-2K total score >= 10 at screening (HDA subjects) and evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	28	35	24
Units: Subjects	18	19	23	15

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8364
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	3.71

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8287
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	3.45

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7621
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	4.16

Secondary: DBPC: Number of Subjects With a Sustained Reduction of Oral Corticosteroids (OCS) Dose to 7.5 mg Prednisone Equivalent per day or Less With Response Based on SRI-4 at Week 52 in Serologically Active Subgroup

End point title	DBPC: Number of Subjects With a Sustained Reduction of Oral Corticosteroids (OCS) Dose to 7.5 mg Prednisone Equivalent per day or Less With Response Based on SRI-4 at Week 52 in Serologically Active Subgroup

End point description:

SRI-4 response was defined as >= 4-point reduction in SLEDAI-2K total score, no new BILAG A and no more than 1 new BILAG B domain score, no worsening (<10 % increase) from baseline in PGA of Disease Activity and no treatment failure. SLEDAI-2K assessment consists of 24 items with total score of 0(no symptoms) to 105 (presence of all defined symptoms) with higher scores representing increased disease activity. BILAG Index: assessing clinical signs, symptoms, or laboratory parameters related to SLE, divided into 9 organ systems. For each organ system A=severe disease, B=moderate disease, C=mild stable disease, D=inactive, but previously active, E=inactive and never affected. The PGA assess disease activity on a visual analogue scale = from very well(0)-very poor(100). The mITT analysis set was used. Here, "Number of subjects analyzed" signifies subjects with positive antidsDNA and/or low complement levels at screening (Serologically active subgroup) were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	33	32	34
Units: Subjects	21	25	22	25

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8464
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	3.31

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9988
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	3.74

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.417
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	2.12

Secondary: DBPC: Number of Subjects With Lupus Low Disease Activity State (LLDAS) at Week 52

End point title	DBPC: Number of Subjects With Lupus Low Disease Activity State (LLDAS) at Week 52

End point description:

Lupus low disease activity state will be measured as: SLEDAI-2K <= 4; No activity in any major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever); No new features of disease activity compared with the previous assessment; Prednisone-equivalent <= 7.5 milligram per day; Unchanged background immunosuppressive therapy. The mITT analysis set included all randomized subjects who had received at least one dose of IMP (Evobrutinib or placebo) and have at least one Baseline and one post Baseline disease assessment among the following: SFI, SLEDAI 2K, PGA, BILAG 2004, CLASI.

End point type	Secondary

End point timeframe:

Week 52

End point values	DBPC: Placebo	DBPC: M2951 25 mg QD	DBPC: M2951 75 mg QD	DBPC: M2951 50 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	115	116	114
Units: Subjects	29	32	35	29

Statistical analyses

Statistical analysis title	Placebo and M2951 25 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 25 mg QD
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.697
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	2.04

Statistical analysis title	Placebo and M2951 75 mg QD
Comparison groups	DBPC: Placebo v DBPC: M2951 75 mg QD
Number of subjects included in analysis	230
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3234
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.42

Statistical analysis title	Placebo and M2951 50 mg BID
Comparison groups	DBPC: Placebo v DBPC: M2951 50 mg BID

Number of subjects included in analysis	228
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9846
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.82

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Double-Blind Placebo-Controlled: Baseline up to Week 56 Open-Label Long-Term Extension Period: Up to Week 108	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1/23.0

Reporting groups	
Reporting group title	M2951 25 mg QD
Reporting group description: Participants received 25 milligrams (mg) of M2951 orally once daily (QD) for 52 weeks.	
Reporting group title	Placebo
Reporting group description: Participants received placebo matched to M2951 orally for 52 weeks.	
Reporting group title	M2951 50 mg BID
Reporting group description: Participants received 50 mg of M2951 orally twice daily (BID) for 52 weeks.	
Reporting group title	Placebo/ M2951 50 mg BID
Reporting group description: Subjects who completed Double-blind Placebo-controlled period and entered in long-term extension period, received 50 mg of M2951 orally twice daily (BID) for 104 weeks.	
Reporting group title	M2951 25 mg QD/ M2951 50 mg BID
Reporting group description: Subjects who completed Double-blind M2951 25mg QD period and entered in long-term extension period, received 50 mg of M2951 orally twice daily (BID) for 104 weeks.	
Reporting group title	M2951 75 mg QD
Reporting group description: Participants received 75 mg of M2951 orally QD for 52 weeks.	
Reporting group title	M2951 50 mg BID/ M2951 50 mg BID
Reporting group description: Subjects who completed Double-blind M2951 50 mg BID period and entered in long-term extension period, continued to receive 50 mg of M2951 orally twice daily (BID) for 104 weeks.	
Reporting group title	M2951 75 mg QD/ M2951 50 mg BID
Reporting group description: Subjects who completed Double-blind M2951 75 mg QD period and entered in long-term extension period, received 50 mg of M2951 orally twice daily (BID) for 104 weeks.	

Serious adverse events	M2951 25 mg QD	Placebo	M2951 50 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 118 (11.02%)	10 / 117 (8.55%)	9 / 117 (7.69%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Papillary thyroid cancer			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant hypertension			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Hypotension			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	2 / 118 (1.69%)	0 / 117 (0.00%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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

Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Metrorrhagia			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Liver function test increased			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			

subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Injury, poisoning and procedural complications			
Ligament injury			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis lupus			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 118 (0.85%)	2 / 117 (1.71%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Presyncope			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Syncope			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Cerebral infarction			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral venous sinus thrombosis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Bone marrow failure			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anemia			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis, unspecified, except mesenteric			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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

Lupus enteritis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Dental cyst			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Diarrhoea			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
Abdominal adhesions			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Skin and subcutaneous tissue disorders			
Cutaneous vasculitis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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

Dermatosis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Dermatitis contact			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Lupus nephritis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Back pain			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intervertebral disc protrusion			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Osteoarthritis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Osteonecrosis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Systemic lupus erythematosus			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of jaw			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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
SLE arthritis			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Otitis media			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter sepsis			

subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Cellulitis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Diverticulitis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Gastroenteritis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Giardiasis			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Pneumonia			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Soft tissue infection			

subjects affected / exposed	1 / 118 (0.85%)	0 / 117 (0.00%)	0 / 117 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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			
subjects affected / exposed	0 / 118 (0.00%)	1 / 117 (0.85%)	0 / 117 (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, site not specified			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subperiosteal abscess			

subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo/ M2951 50 mg BID	M2951 25 mg QD/ M2951 50 mg BID	M2951 75 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 62 (8.06%)	5 / 69 (7.25%)	11 / 117 (9.40%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant hypertension			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			

subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine polyp			
subjects affected / exposed	0 / 62 (0.00%)	1 / 69 (1.45%)	0 / 117 (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
Metrorrhagia			
subjects affected / exposed	0 / 62 (0.00%)	1 / 69 (1.45%)	0 / 117 (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
Ovarian cyst			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Liver function test increased			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament injury			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			

subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis lupus			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
Cerebral venous sinus thrombosis			

subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
Blood and lymphatic system disorders			
Bone marrow failure			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anemia			
subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
Leukopenia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis, unspecified, except mesenteric			
subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Eye disorders			
Cataract			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus enteritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental cyst			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal adhesions			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
Skin and subcutaneous tissue disorders			
Cutaneous vasculitis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatosis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis contact			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 62 (0.00%)	1 / 69 (1.45%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus nephritis			
subjects affected / exposed	1 / 62 (1.61%)	1 / 69 (1.45%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
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 chest pain			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			

subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic lupus erythematosus			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of jaw			
subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
SLE arthritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Otitis media			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter sepsis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Giardiasis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 62 (0.00%)	2 / 69 (2.90%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			

subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
Urinary tract infection, site not specified			
subjects affected / exposed	0 / 62 (0.00%)	2 / 69 (2.90%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	0 / 117 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subperiosteal abscess			
subjects affected / exposed	1 / 62 (1.61%)	0 / 69 (0.00%)	0 / 117 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	M2951 50 mg BID/ M2951 50 mg BID	M2951 75 mg QD/ M2951 50 mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 72 (9.72%)	5 / 80 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant hypertension			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 72 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			

subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 72 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 72 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Liver function test increased			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			

subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ligament injury			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericarditis lupus			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 72 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Headache			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous sinus thrombosis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Bone marrow failure			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anemia			

subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis, unspecified, except mesenteric			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus enteritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental cyst			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal adhesions			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Cutaneous vasculitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatosis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis contact			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus nephritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 72 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SLE arthritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Otitis media			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter sepsis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Giardiasis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 72 (1.39%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			

subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection, site not specified			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 72 (0.00%)	1 / 80 (1.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			

subjects affected / exposed	1 / 72 (1.39%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subperiosteal abscess			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	M2951 25 mg QD	Placebo	M2951 50 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 118 (72.03%)	76 / 117 (64.96%)	78 / 117 (66.67%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 118 (6.78%)	3 / 117 (2.56%)	6 / 117 (5.13%)
occurrences (all)	8	3	6
Lipase increased			
subjects affected / exposed	4 / 118 (3.39%)	2 / 117 (1.71%)	6 / 117 (5.13%)
occurrences (all)	4	2	6
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 118 (6.78%)	3 / 117 (2.56%)	4 / 117 (3.42%)
occurrences (all)	8	3	4
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 118 (3.39%)	6 / 117 (5.13%)	7 / 117 (5.98%)
occurrences (all)	4	6	7
Amylase increased			
subjects affected / exposed	2 / 118 (1.69%)	5 / 117 (4.27%)	8 / 117 (6.84%)
occurrences (all)	2	5	8

Transaminases increased			
subjects affected / exposed	3 / 118 (2.54%)	3 / 117 (2.56%)	6 / 117 (5.13%)
occurrences (all)	3	3	6
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 118 (5.08%)	0 / 117 (0.00%)	1 / 117 (0.85%)
occurrences (all)	6	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 118 (14.41%)	20 / 117 (17.09%)	17 / 117 (14.53%)
occurrences (all)	17	20	17
Dizziness			
subjects affected / exposed	5 / 118 (4.24%)	3 / 117 (2.56%)	6 / 117 (5.13%)
occurrences (all)	5	3	6
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	4 / 118 (3.39%)	9 / 117 (7.69%)	2 / 117 (1.71%)
occurrences (all)	4	9	2
Neutropenia			
subjects affected / exposed	1 / 118 (0.85%)	4 / 117 (3.42%)	6 / 117 (5.13%)
occurrences (all)	1	4	6
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	7 / 118 (5.93%)	5 / 117 (4.27%)	7 / 117 (5.98%)
occurrences (all)	7	5	7
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 118 (10.17%)	11 / 117 (9.40%)	10 / 117 (8.55%)
occurrences (all)	12	11	10
Nausea			
subjects affected / exposed	8 / 118 (6.78%)	7 / 117 (5.98%)	5 / 117 (4.27%)
occurrences (all)	8	7	5
Vomiting			
subjects affected / exposed	9 / 118 (7.63%)	4 / 117 (3.42%)	3 / 117 (2.56%)
occurrences (all)	9	4	3
Abdominal pain upper			

subjects affected / exposed	6 / 118 (5.08%)	5 / 117 (4.27%)	5 / 117 (4.27%)
occurrences (all)	6	5	5
Abdominal pain			
subjects affected / exposed	7 / 118 (5.93%)	3 / 117 (2.56%)	5 / 117 (4.27%)
occurrences (all)	7	3	5
Gastritis			
subjects affected / exposed	6 / 118 (5.08%)	3 / 117 (2.56%)	4 / 117 (3.42%)
occurrences (all)	6	3	4
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 118 (1.69%)	6 / 117 (5.13%)	0 / 117 (0.00%)
occurrences (all)	2	6	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	4 / 118 (3.39%)	3 / 117 (2.56%)	9 / 117 (7.69%)
occurrences (all)	4	3	9
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	21 / 118 (17.80%)	16 / 117 (13.68%)	21 / 117 (17.95%)
occurrences (all)	21	16	21
Nasopharyngitis			
subjects affected / exposed	13 / 118 (11.02%)	8 / 117 (6.84%)	7 / 117 (5.98%)
occurrences (all)	13	8	7
Upper respiratory tract infection			
subjects affected / exposed	15 / 118 (12.71%)	12 / 117 (10.26%)	8 / 117 (6.84%)
occurrences (all)	15	12	8
Pharyngitis			
subjects affected / exposed	5 / 118 (4.24%)	8 / 117 (6.84%)	4 / 117 (3.42%)
occurrences (all)	5	8	4
Gastroenteritis			
subjects affected / exposed	4 / 118 (3.39%)	6 / 117 (5.13%)	2 / 117 (1.71%)
occurrences (all)	4	6	2
Herpes zoster			
subjects affected / exposed	2 / 118 (1.69%)	2 / 117 (1.71%)	0 / 117 (0.00%)
occurrences (all)	2	2	0
Bronchitis			

subjects affected / exposed	0 / 118 (0.00%)	0 / 117 (0.00%)	0 / 117 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Placebo/ M2951 50 mg BID	M2951 25 mg QD/ M2951 50 mg BID	M2951 75 mg QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 62 (35.48%)	34 / 69 (49.28%)	75 / 117 (64.10%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 62 (8.06%)	4 / 69 (5.80%)	6 / 117 (5.13%)
occurrences (all)	5	4	6
Lipase increased			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	6 / 117 (5.13%)
occurrences (all)	0	0	6
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 62 (4.84%)	4 / 69 (5.80%)	3 / 117 (2.56%)
occurrences (all)	3	4	3
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 62 (4.84%)	3 / 69 (4.35%)	4 / 117 (3.42%)
occurrences (all)	3	3	4
Amylase increased			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	4 / 117 (3.42%)
occurrences (all)	0	0	4
Transaminases increased			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	3 / 117 (2.56%)
occurrences (all)	0	0	3
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	4 / 117 (3.42%)
occurrences (all)	0	0	4
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 62 (1.61%)	7 / 69 (10.14%)	19 / 117 (16.24%)
occurrences (all)	1	7	19
Dizziness			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	4 / 117 (3.42%)
occurrences (all)	0	0	4

Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	6 / 117 (5.13%)
occurrences (all)	0	0	6
Neutropenia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	2 / 117 (1.71%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	4 / 62 (6.45%)	0 / 69 (0.00%)	9 / 117 (7.69%)
occurrences (all)	4	0	9
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 62 (4.84%)	5 / 69 (7.25%)	17 / 117 (14.53%)
occurrences (all)	3	5	17
Nausea			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	9 / 117 (7.69%)
occurrences (all)	0	0	9
Vomiting			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	8 / 117 (6.84%)
occurrences (all)	0	0	8
Abdominal pain upper			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	8 / 117 (6.84%)
occurrences (all)	0	0	8
Abdominal pain			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	3 / 117 (2.56%)
occurrences (all)	0	0	3
Gastritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	3 / 117 (2.56%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	1 / 117 (0.85%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Back Pain			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	5 / 117 (4.27%)
occurrences (all)	0	0	5
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 62 (6.45%)	7 / 69 (10.14%)	26 / 117 (22.22%)
occurrences (all)	4	7	26
Nasopharyngitis			
subjects affected / exposed	5 / 62 (8.06%)	5 / 69 (7.25%)	15 / 117 (12.82%)
occurrences (all)	5	5	15
Upper respiratory tract infection			
subjects affected / exposed	3 / 62 (4.84%)	6 / 69 (8.70%)	6 / 117 (5.13%)
occurrences (all)	3	6	6
Pharyngitis			
subjects affected / exposed	0 / 62 (0.00%)	3 / 69 (4.35%)	4 / 117 (3.42%)
occurrences (all)	0	3	4
Gastroenteritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	2 / 117 (1.71%)
occurrences (all)	0	0	2
Herpes zoster			
subjects affected / exposed	0 / 62 (0.00%)	0 / 69 (0.00%)	6 / 117 (5.13%)
occurrences (all)	0	0	6
Bronchitis			
subjects affected / exposed	0 / 62 (0.00%)	4 / 69 (5.80%)	0 / 117 (0.00%)
occurrences (all)	0	4	0

Non-serious adverse events	M2951 50 mg BID/ M2951 50 mg BID	M2951 75 mg QD/ M2951 50 mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 72 (31.94%)	35 / 80 (43.75%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 72 (2.78%)	1 / 80 (1.25%)	
occurrences (all)	2	1	
Lipase increased			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase			

increased			
subjects affected / exposed	2 / 72 (2.78%)	1 / 80 (1.25%)	
occurrences (all)	2	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 72 (5.56%)	1 / 80 (1.25%)	
occurrences (all)	4	1	
Amylase increased			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Transaminases increased			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 72 (6.94%)	2 / 80 (2.50%)	
occurrences (all)	5	2	
Dizziness			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	0 / 72 (0.00%)	2 / 80 (2.50%)	
occurrences (all)	0	2	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	2 / 72 (2.78%)	7 / 80 (8.75%)	
occurrences (all)	2	7	
Nausea			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Gastritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	6 / 72 (8.33%)	7 / 80 (8.75%)	
occurrences (all)	6	7	
Nasopharyngitis			
subjects affected / exposed	5 / 72 (6.94%)	7 / 80 (8.75%)	
occurrences (all)	5	7	
Upper respiratory tract infection			
subjects affected / exposed	0 / 72 (0.00%)	3 / 80 (3.75%)	
occurrences (all)	0	3	

Pharyngitis			
subjects affected / exposed	1 / 72 (1.39%)	6 / 80 (7.50%)	
occurrences (all)	1	6	
Gastroenteritis			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	0 / 72 (0.00%)	0 / 80 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	3 / 72 (4.17%)	5 / 80 (6.25%)	
occurrences (all)	3	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2017	- Added of text describing the Study Steering Committee. - Provided updated safety and efficacy information from other clinical studies, and potential risks associated with the IMP - Provided additional safety data in the benefit-risk analysis - Added a Japanese cohort to the study - Added additional rescreening information - Modified inclusion criteria regarding contraceptive use in male subjects based on newly available data and provided clarifications regarding vaccination and background standard of care - Modified exclusion criteria to excluded JAK inhibitors and BTK inhibitors - Corrected Common Terminology Criteria for Adverse Events (CTCAE) laboratory parameters - Clarified that medical marijuana use is not excluded.
31 August 2017	- Study eligibility, and - Modified inclusion and exclusion criteria were added.
20 November 2017	Included all of the country specific changes in the global amended protocol, included a fasting requirement prior to dosing for all subjects in all countries, and added new safety information and additional visits for liver function test (LFT) monitoring.
05 January 2018	- Revisions of the criteria for withdrawal the IMP based on the outcome of an IDMC meeting; - Addition of visit window (±3) for the Visits 6, 10, and 14 and Correction of an inconsistency about the vital signs measurement position.
08 February 2018	-Provided additional rationale for dose selection, updated safety information from other clinical studies, and potential risks associated with the IMP. - Modified inclusion and exclusion criteria.
22 May 2018	- A Long term extension (LTE) period was added into the study, including 2 new schedule of activities (SoAs), and an additional study figure. - Stopping rules modified due to analysis of additional safety data. - Exclusion modified to permit low dose aspirin after medical review.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported