Clinical trial results:
A Phase II, Open-Label Extension Study of Patients Previously Enrolled in Study GA30044 to Evaluate the Long-Term Safety and Efficacy of GDC-0853 in Patients With Moderate to Severe Active Systemic Lupus Erythematosus

Summary

EudraCT number	2017-001764-37
Trial protocol	GB ES PT BG
Global end of trial date	20 November 2019

Results information

Result version number	v2 (current)
This version publication date	06 January 2021
First version publication date	05 November 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	GA30066

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03407482
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 November 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 November 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and efficacy of GDC-0853

Protection of trial subjects:

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

Background therapy:

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

Evidence for comparator: -

Actual start date of recruitment	09 January 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 18
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	Brazil: 41
Country: Number of subjects enrolled	Chile: 28
Country: Number of subjects enrolled	Colombia: 25
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Mexico: 12
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	160
EEA total number of subjects	14

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	154
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 50 centers in 11 countries.

Pre-assignment

Screening details:

160 subjects were enrolled into this OLE study and were included in the ITT and Safety populations.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	GDC-0853 (200mg) BID

Arm description:

Subjects previously enrolled in the parent GA30044 Study, now received GDC-0853 (200mg) orally twice daily (BID).

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

Dosage and administration details:

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

Number of subjects in period 1	GDC-0853 (200mg) BID
Started	160
Completed	29
Not completed	131
Disease Relapse	1
Consent withdrawn by subject	6
Data Entry Error	1
Adverse event, non-fatal	12
Study Terminated By Sponsor	106
Non-Compliance With Study Drug	1
Pregnancy	2
Lost to follow-up	1
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	GDC-0853 (200mg) BID
Reporting group description:	
Subjects previously enrolled in the parent GA30044 Study, now received GDC-0853 (200mg) orally twice daily (BID).	

Reporting group values	GDC-0853 (200mg) BID	Total	
Number of subjects	160	160	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	154	154	
From 65-84 years	6	6	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	42.8		
standard deviation	± 11.5	-	
Sex: Female, Male			
Units:			
Female	155	155	
Male	5	5	
Race/Ethnicity, Customized			
Ethnicity			
Units: Subjects			
Hispanic or Latino	117	117	
Not Hispanic or Latino	42	42	
Not Stated	1	1	
Race/Ethnicity, Customized			
Race			
Units: Subjects			
American Indian or Alaska native	24	24	
Asian	5	5	
Black or African American	22	22	
Multiple	5	5	
White	104	104	

End points

End points reporting groups

Reporting group title	GDC-0853 (200mg) BID

Reporting group description:

Subjects previously enrolled in the parent GA30044 Study, now received GDC-0853 (200mg) orally twice daily (BID).

Primary: Percentage of Subjects With Adverse Events (AEs)

End point title	Percentage of Subjects With Adverse Events (AEs)[1]

End point description:

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

End point type	Primary

End point timeframe:

Baseline up until 8 weeks after the last dose of study drug (up to 56 weeks)

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: No statistical analyses were performed, as this study has only 1 arm.

End point values	GDC-0853 (200mg) BID			
Subject group type	Reporting group			
Number of subjects analysed	160			
Units: Percentage of Subjects				
number (not applicable)	64.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Systemic Lupus Erythematosus Responder-4 Index (SRI-4) up to Week 48

End point title	Systemic Lupus Erythematosus Responder-4 Index (SRI-4) up to Week 48

End point description:

The SRI-4 measures reduction in SLE disease activity and is a composite measure that includes the SLE Disease Activity Index (SLEDAI-2K), British Isles Lupus Activity Group (BILAG) 2004 and Physician Global Assessment. It is defined as: 1) Reduction of ≥4 points from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score; 2) no new British Isles Lupus Assessment Group (BILAG) A or no more than 1 new BILAG B disease activity scores and 3) no worsening (defined as an increase of ≥0.3 points [10 mm] from baseline) in the Physician's Global Assessment of Disease Activity. The score range is from 0 to 100, with higher scores indicating greater disease activity. No data was collected at all due to no subjects being evaluated at all, because of early termination of this study due to fenebrutinib not demonstrating improved efficacy compared to placebo across secondary or exploratory endpoints in the parent study (Study GA30044).

End point type	Secondary

End point timeframe:

Baseline up to Week 48

End point values	GDC-0853 (200mg) BID			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Percentage of Subjects				

Notes:

[2] - Not evaluated due to early termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration-Time Curve From Time 0 to Time t (AUC0-t,ss) of GDC-0853 at Steady State

End point title	Area Under the Concentration-Time Curve From Time 0 to Time t (AUC0-t,ss) of GDC-0853 at Steady State

End point description:

Population PK model estimated AUC of GDC-0853 From Time 0 to Time t (AUC0-t) at steady-state. AUC was measured in Nanograms (ng) per millilitre(mL)*hour (hr). Please note that for this Outcome Measure, incomplete PK data was collected as a result of early termination of the study which meant that data for the (AUC0-t,ss) parameter could not be generated via the Population PK model.

End point type	Secondary

End point timeframe:

Pre-dose (0 hour [hr]) at Weeks 0, 24, 48, at unscheduled or flare or early termination visit (up to Week 56)

End point values	GDC-0853 (200mg) BID			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Ng/mL*(hr)				
arithmetic mean (standard deviation)	()			

Notes:

[3] - Not evaluated due to early termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Plasma Concentration of GDC-0853 at Steady State (Ctrough,ss)

End point title	Minimum Plasma Concentration of GDC-0853 at Steady State (Ctrough,ss)

End point description:

Population PK model estimated minimal plasma concentration (Ctrough) of GDC-0853 at steady-state (ss). Please note that for this Outcome Measure, incomplete PK data was collected as a result of early termination of the study which meant that data for the (Ctrough,ss) parameter could not be generated via the Population PK model.

End point type	Secondary

End point timeframe:

Pre-dose (0 hr) at Weeks 0, 24, 48, at unscheduled or flare or early termination visit (up to Week 56)

End point values	GDC-0853 (200mg) BID			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: ng/mL				
arithmetic mean (standard deviation)	()			

Notes:

[4] - Not evaluated due to early termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Decay Half-Life of GDC-0853 at Steady State (t1/2,ss)

End point title	Plasma Decay Half-Life of GDC-0853 at Steady State (t1/2,ss)

End point description:

Population PK model estimated plasma decay half life of GDC-0853 at steady-state. Please note that for this Outcome Measure, incomplete PK data was collected as a result of early termination of the study which meant that data for the (t1/2,ss) parameter could not be generated via the Population PK model.

End point type	Secondary

End point timeframe:

Pre-dose (0 hr) at Weeks 0, 24, 48, at unscheduled or flare or early termination visit (up to Week 56)

End point values	GDC-0853 (200mg) BID			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: hr				
arithmetic mean (standard deviation)	()			

Notes:

[5] - Not evaluated due to early termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Oral Clearance of GDC-0853 at Steady State (CL/F,ss)

End point title	Apparent Oral Clearance of GDC-0853 at Steady State (CL/F,

	ss)

End point description:

Population PK model estimated apparent oral clearance of GDC-0853 at steady-state. Please note that for this Outcome Measure, incomplete PK data was collected as a result of early termination of the study which meant that data for the (CL/F,ss) parameter could not be generated via the Population PK model.

End point type	Secondary

End point timeframe:

Pre-dose (0 hr) at Weeks 0, 24, 48, at unscheduled or flare or early termination visit (up to Week 56)

End point values	GDC-0853 (200mg) BID			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: L/hr				
arithmetic mean (standard deviation)	()			

Notes:

[6] - Not evaluated due to early termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up until 8 weeks after the last dose of study drug (up to 56 weeks)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	GDC-0853 (200mg) BID
Reporting group description:	
Subjects previously enrolled in the parent GA30044 Study, now received GDC-0853 (200mg) orally twice daily (BID).	

Serious adverse events	GDC-0853 (200mg) BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 160 (2.50%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
SYSTEMIC LUPUS ERYTHEMATOSUS			
subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
CELLULITIS			
subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INFECTIVE TENOSYNOVITIS			

subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 160 (0.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	GDC-0853 (200mg) BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 160 (19.38%)		
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	9 / 160 (5.63%)		
occurrences (all)	9		
Infections and infestations			
NASOPHARYNGITIS			
subjects affected / exposed	13 / 160 (8.13%)		
occurrences (all)	14		
URINARY TRACT INFECTION			
subjects affected / exposed	15 / 160 (9.38%)		
occurrences (all)	15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was ended early due to the lack of efficacy seen in the parent study GA30044.

Notes: