Clinical trial results:
An open label phase 2a trial assessing the clinical effect and safety of RO5459072 in moderate to severe psoriasis.

Summary

EudraCT number	2018-002446-36
Trial protocol	DE
Global end of trial date	25 June 2019

Results information

Result version number	v1 (current)
This version publication date	08 July 2020
First version publication date	08 July 2020

Trial information

Trial identification

Sponsor protocol code	BP40635

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche, Ltd.
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche, Ltd., +41 616878333, genentech@druginfo.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 June 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the clinical effect of oral RO5459072 in adult subjects with moderate to severe psorisis.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 December 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

Notes:

Subjects enrolled per age group

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 30 subjects were enrolled in the study.

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	RO5459072 100 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Petesicatib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Two 50 mg capsules of RO5459072 (total of 100 mg) BID (twice a day) for 12 weeks

Number of subjects in period 1	RO5459072 100 mg
Started	30
Completed	17
Not completed	13
Study terminated by Sponsor	10
Adverse Event	2
Early termination by Sponsor	1

Baseline characteristics

Reporting groups	
Reporting group title	RO5459072 100 mg

Reporting group description: -

Reporting group values	RO5459072 100 mg	Total	
Number of subjects	30	30	
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)	27	27	
From 65-84 years	3	3	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	48.7		
standard deviation	± 11.0	-	
Gender Categorical Units: Subjects			
Female	3	3	
Male	27	27	

End points

End points reporting groups

Reporting group title	RO5459072 100 mg

Reporting group description: -

Primary: Percentage of subjects that achieved a psoriasis area and severity index (PASI)75 (PASI75) response after twelve weeks of treatment

End point title	Percentage of subjects that achieved a psoriasis area and severity index (PASI)75 (PASI75) response after twelve weeks of treatment[1]

End point description:

The PASI score was used as a measure of disease severity. The PASI was also used as a measure for the efficacy of study treatments, either as a continuous score, or as the percentage of subjects in the trial who achieve a defined level of improvement.

End point type	Primary

End point timeframe:

Week 12

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 formal statistical analyses were performed as the study was terminated for futility.

End point values	RO5459072 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	17[2]			
Units: Percentage of subjects				
number (not applicable)	0			

Notes:

[2] - No patients achieved a PASI75 response after twelve weeks of treatment.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects that achieve a PASI50, PASI75, and PASI90 response of RO5459072 after six weeks and twelve weeks of treatment, and four weeks after completion of treatment

End point title	Number of subjects that achieve a PASI50, PASI75, and PASI90 response of RO5459072 after six weeks and twelve weeks of treatment, and four weeks after completion of treatment

End point description:

The PASI score was used as a measure of disease severity. The PASI was also used as a measure for the efficacy of study treatments, either as a continuous score, or as the percentage of subjects in the trial who achieve a defined level of improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 6, Week 12, Week 4 after completion of treatment

End point values	RO5459072 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Number of subjects				
number (not applicable)				
PASI50 Week 6	3			
PASI50 Week 12	1			
PASI50 Follow up	0			
PASI75 Week 6	0			
PASI75 Week 12	0			
PASI75 Follow up	0			
PASI90 Week 6	0			
PASI90 Week 12	0			
PASI90 Follow up	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of PASI from baseline after six weeks and twelve weeks of treatment, and four weeks after completion of treatment

End point title	Change of PASI from baseline after six weeks and twelve weeks of treatment, and four weeks after completion of treatment

End point description:

The PASI score was used as a measure of disease severity. The PASI was also used as a measure for the efficacy of study treatments, either as a continuous score, or as the proportion of patients in the trial who achieve a defined level of improvement.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 6, Week 12, Week 4 after completion of treatment

End point values	RO5459072 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Units on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[3] - This endpoint was not analyzed due to early study termination based on lack of efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: Change of static Investigator’s global assessment (sIGA) after six weeks and twelve weeks of treatment, and four weeks after completion of treatment

End point title	Change of static Investigator’s global assessment (sIGA) after six weeks and twelve weeks of treatment, and four weeks after completion of treatment

End point description:

The Investigator’s Global Assessment (IGA, also known as Physician’s Global Assessment, PGA) is a tool that provided a subjective evaluation of the overall severity of psoriasis using a 6-point ordinal scale ranging from “clear” to “very severe." The static IGA (sIGA) was used in this study and measured the Investigator’s impression of disease severity at a single time-point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 6, Week 12, Week 4 after completion of treatment

End point values	RO5459072 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Number of subjects				
number (not applicable)				
Baseline Mild	2			
Baseline Moderate	15			
Baseline Severe	14			
Baseline Very Severe	0			
Week 6 Mild	0			
Week 6 Moderate	17			
Week 6 Severe	5			
Week 6 Very Severe	1			
Week 12 Mild	2			
Week 12 Moderate	4			
Week 12 Severe	3			
Week 12 Very Severe	0			
Follow up Mild	3			
Follow up Moderate	20			
Follow up Severe	6			
Follow up Very Severe	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Dermatology Life Quality Index (DLQI) after six weeks and twelve weeks of treatment, and four weeks after completion of treatment.

End point title	Change in Dermatology Life Quality Index (DLQI) after six weeks and twelve weeks of treatment, and four weeks after completion of treatment.

End point description:

Subjects were to answer 10 questions considering their Quality of Life (QoL) during the previous week on a 4-point scale. The total DLQI score represent the sum of the scores for each question, and ranges from 0 to 30, with higher scores reflecting worse QoL.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 6, Week 12, Week 4 after completion of treatment

End point values	RO5459072 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Units on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[4] - This endpoint was not analyzed due to early study termination based on lack of efficacy.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with adverse events (AEs)

End point title	Percentage of subjects with adverse events (AEs)

End point description:

AEs were defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Grading was completed according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE).

End point type	Secondary

End point timeframe:

Up to Week 20

End point values	RO5459072 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of subjects				
number (not applicable)	83.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations of RO5459072

End point title	Plasma Concentrations of RO5459072

End point description:

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 6 and Week 12

End point values	RO5459072 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: nanograms per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
Baseline PT3H (n=28)	423.60 (± 331.95)			
Week 6 -PT2H (n=25)	1196.30 (± 549.22)			
Week 6 PT2H (n=22)	1245.95 (± 578.33)			
Week 6 PT4H (n=22)	1492.27 (± 570.51)			
Week 6 PTH6 (n=22)	1539.73 (± 460.58)			
Week 12 -PT2H (n=9)	1289.33 (± 613.75)			
Week 12 PT3H (n=9)	1508.22 (± 745.10)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 20	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	RO5459072 100 mg
Reporting group description:	
Subjects received two 50 mg capsules of RO5459072 (total of 100 mg) BID (total daily dose of 200 mg) for 12 weeks with or after food intake.	

Serious adverse events	RO5459072 100 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Skin infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	RO5459072 100 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 30 (63.33%)		
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
General disorders and administration site conditions			
Chills			

subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2 2 / 30 (6.67%) 2		
Gastrointestinal disorders Dry mouth subjects affected / exposed occurrences (all)	 2 / 30 (6.67%) 2		
Skin and subcutaneous tissue disorders Pruritus generalised subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Psoriasis subjects affected / exposed occurrences (all) Skin exfoliation subjects affected / exposed occurrences (all)	 3 / 30 (10.00%) 3 7 / 30 (23.33%) 8 3 / 30 (10.00%) 3 3 / 30 (10.00%) 3 2 / 30 (6.67%) 3		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	 3 / 30 (10.00%) 3		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 7 / 30 (23.33%) 9		

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 terminated early because no efficacy was observed.

Notes: