Clinical trial results: randomized, double-blind, placebo-controlled, parallel group study evaluating efficacy and safety of QAW039 in the treatment of patients with moderate to severe atopic dermatitis

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-005321-78
Trial protocol	AT DE BE NL
Global end of trial date	12 November 2014

Results information

Result version number	v1 (current)
This version publication date	28 May 2016
First version publication date	28 May 2016

Trial information

Trial identification

Sponsor protocol code	CQAW039X2201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01785602
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111 x,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111 x,

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	12 November 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of once daily doses of QAW039 as measured by Eczema Area and Severity Index (EASI) after 12 weeks of treatment relative to placebo in adult patients with moderate to severe atopic dermatitis (AD); To evaluate safety and tolerability of once daily doses of QAW039 over 12 weeks of treatment in adult patients with moderate to severe AD as expressed in terms of frequency of adverse events (AEs).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 June 2013
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	Australia: 19
Country: Number of subjects enrolled	Austria: 8
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	Germany: 24
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	South Africa: 2
Worldwide total number of subjects	103
EEA total number of subjects	82

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	101
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Following a screening period of up to 28 days (from Day -28) and a baseline period (Day 1), patients who met the inclusion and exclusion criteria were randomized to receive QAW039 450 mg (3 x 150 mg capsules) administered orally once daily or matching placebo for 12 weeks.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	QAW039

Arm description:

Participants received QAW039 450 mg daily by mouth.

Arm type	Experimental
Investigational medicinal product name	QAW039
Investigational medicinal product code	QAW039
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

450 mg by mouth once daily

Arm title	Placebo

Arm description:

Participants received matching placebo to QAW039.

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

Dosage and administration details:

matching placebo to QAW039 given by mouth once daily

Number of subjects in period 1	QAW039	Placebo
Started	76	27
Completed	63	18
Not completed	13	9
Consent withdrawn by subject	2	-
Adverse event, non-fatal	3	5
Administrative problems	7	3
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	QAW039
Reporting group description:	
Participants received QAW039 450 mg daily by mouth.	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo to QAW039.	

Reporting group values	QAW039	Placebo	Total
Number of subjects	76	27	103
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	74	27	101
From 65-84 years	2	0	2
85 years and over	0	0	0
Age Continuous | Units: Years			
arithmetic mean	35.5	38.7	
standard deviation	± 13.08	± 9.95	-
Gender, Male/Female Units: Participants			
Female	27	12	39
Male	49	15	64

End points

End points reporting groups

Reporting group title	QAW039
Reporting group description:	
Participants received QAW039 450 mg daily by mouth.	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo to QAW039.	

Primary: Change from baseline in Eczema Area and Severity Index (EASI)

End point title	Change from baseline in Eczema Area and Severity Index (EASI)[1]

End point description:

Investigators assessed presence and severity of erythema, induration/papulation, excoriation, and lichenification in four body areas: head/neck (H), upper limbs (UL), trunk (T), and lower limbs (LL). Investigators assigned a severity score from 0 – 3 for each area (none=0, mild=1, moderate=2, and severe=3). Investigators could assign half-points. Investigators also assigned an area score from 0 (no atopic dermatitis lesion in the area) to 6 (entire area is affected) for each area. The weighting factor was 0.1 for head/neck, 0.2 for upper limbs, 0.3 for trunk, and 0.4 for lower limbs. The total body score for each body region was obtained by multiplying the sum of the severity scores of the four key signs by the area score, then multiplying the result by the constant weighted value assigned to that body region. The sum of these scores gave the EASI total, ranging from 0 to 72. A higher score represented greater disease severity. A negative change from baseline indicates improvement.

End point type	Primary

End point timeframe:

Baseline, 12 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 analysis was planned for this outcome measure.

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	27		
Units: Score on a scale				
arithmetic mean (standard error)	-8.65 (± 0.01)	-6.95 (± 0.017)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Eczema Area and Severity Index

End point title	Change from baseline in Eczema Area and Severity Index

End point description:

Investigators assessed presence and severity of erythema, induration/papulation, excoriation, and lichenification in four body areas: head/neck (H), upper limbs (UL), trunk (T), and lower limbs (LL). Investigators assigned a severity score from 0 – 3 for each area (none=0, mild=1, moderate=2, and severe=3). Investigators could assign half-points. Investigators also assigned an area score from 0 (no

atopic dermatitis lesion in the area) to 6 (entire area is affected) for each area. The weighting factor was 0.1 for head/neck, 0.2 for upper limbs, 0.3 for trunk, and 0.4 for lower limbs. The total body score for each body region was obtained by multiplying the sum of the severity scores of the four key signs by the area score, then multiplying the result by the constant weighted value assigned to that body region. The sum of these scores gave the EASI total, ranging from 0 to 72. A higher score represented greater disease severity. A negative change from baseline indicates improvement.

End point type	Secondary

End point timeframe:

Baseline, 4 weeks, 8 weeks

End point values	QAW039	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76	27		
Units: Score on a scale				
arithmetic mean (standard error)				
Week 4	-6.22 (± 0.01)	-5.89 (± 0.017)		
Week 8	-7.49 (± 0.01)	-5.61 (± 0.017)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo	
Reporting group title	QAW039 450 mg
Reporting group description:	
QAW039 450 mg	

Serious adverse events	Placebo	QAW039 450 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 27 (14.81%)	1 / 76 (1.32%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 27 (0.00%)	1 / 76 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	3 / 27 (11.11%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 76 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Placebo	QAW039 450 mg	
Total subjects affected by non-serious adverse events subjects affected / exposed	16 / 27 (59.26%)	44 / 76 (57.89%)	
Vascular disorders Hot flush subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	0 / 76 (0.00%) 0	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	3 / 76 (3.95%) 3	
Headache subjects affected / exposed occurrences (all)	4 / 27 (14.81%) 8	7 / 76 (9.21%) 7	
Hypoaesthesia subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	0 / 76 (0.00%) 0	
Tension headache subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2	1 / 76 (1.32%) 1	
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	5 / 76 (6.58%) 5	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	4 / 76 (5.26%) 5	
Abdominal pain upper subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 4	3 / 76 (3.95%) 3	

Diarrhoea			
subjects affected / exposed	2 / 27 (7.41%)	10 / 76 (13.16%)	
occurrences (all)	3	11	
Nausea			
subjects affected / exposed	3 / 27 (11.11%)	6 / 76 (7.89%)	
occurrences (all)	4	6	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	9 / 27 (33.33%)	24 / 76 (31.58%)	
occurrences (all)	19	52	
Pruritus			
subjects affected / exposed	2 / 27 (7.41%)	3 / 76 (3.95%)	
occurrences (all)	3	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 27 (7.41%)	1 / 76 (1.32%)	
occurrences (all)	2	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 27 (3.70%)	11 / 76 (14.47%)	
occurrences (all)	1	13	
Oral herpes			
subjects affected / exposed	1 / 27 (3.70%)	4 / 76 (5.26%)	
occurrences (all)	1	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2014	Amendment 1, issued approximately 33 weeks after study start (60 patients enrolled), introduced the following changes: additional 10 ml blood collected at FACS sampling (5 different time points) for PBMC; exploratory analysis of autoantibodies profiles at screening and/or baseline using the same samples as those collected for "Disease and mechanism biomarkers" assessment as a potential stratification biomarker; and potential use of the chip cytometry technology for analyzing skin biopsies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported