Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Repeat-Dose Study of the Efficacy, Safety, Tolerability, and Pharmacodynamics of Subcutaneously-Administered REGN668 in Adult Patients With Extrinsic Moderate-to-Severe Atopic Dermatitis

Summary

EudraCT number	2011-003836-29
Trial protocol	HU DE CZ
Global end of trial date	25 June 2013

Results information

Result version number	v3 (current)
This version publication date	02 December 2019
First version publication date	07 June 2017
Version creation reason	• Correction of full data set Minor corrections

Trial information

Trial identification

Sponsor protocol code	R668-AD-1117

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01548404
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, United States, 10591
Public contact	Clinical Trial Management, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.com
Scientific contact	Clinical Trial Management, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.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 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 June 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the clinical efficacy of repeated subcutaneous (SC) doses of Dupilumab in adult subjects with moderate-to-severe atopic dermatitis (AD).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 March 2012
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	Poland: 23
Country: Number of subjects enrolled	Czech Republic: 11
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 45
Country: Number of subjects enrolled	Hungary: 11
Worldwide total number of subjects	109
EEA total number of subjects	109

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)	106

From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 25 sites in Europe between 03 April 2012 and 25 June 2013. A total of 153 subjects were screened in the study.

Pre-assignment

Screening details:

Out of 153 subjects, 109 were randomized and treated in the study. Subjects were randomized in 1:1 ratio to receive either Dupilumab 300 mg or placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo (for Dupilumab) once weekly for 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo (For Dupilumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single subcutaneous injection altered between back of arms, abdomen and upper thighs.

Arm title	Dupilumab 300 mg

Arm description:

Dupilumab 300 mg once weekly for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Dupilumab 300 mg
Investigational medicinal product code	REGN668/SAR231893
Other name	Dupixent
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single subcutaneous injection altered between back of arms, abdomen and upper thighs

Number of subjects in period 1	Placebo	Dupilumab 300 mg
Started	54	55
Completed	24	41
Not completed	30	14
Other than specified above	-	2
Physician decision	2	1
Consent withdrawn by subject	-	3
Inadequate response to study treatment	23	7
Adverse event	3	1
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo (for Dupilumab) once weekly for 12 weeks.	
Reporting group title	Dupilumab 300 mg
Reporting group description:	
Dupilumab 300 mg once weekly for 12 weeks	

Reporting group values	Placebo	Dupilumab 300 mg	Total
Number of subjects	54	55	109
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 39.4 ± 12.29	 33.7 ± 10.41	 -
Gender categorical Units: Subjects			
Female	27	24	51
Male	27	31	58
Eczema Area and Severity Index (EASI) Score			
The EASI score was used to measure the severity and extent of AD and measures erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper and lower extremities. The total EASI score ranges from 0 (minimum) to 72 (maximum) points, with the higher scores reflecting the worse severity of AD.			
Units: units on a scale arithmetic mean standard deviation	 30.8 ± 13.63	 28.4 ± 13.57	 -
Investigator's Global Assessment (IGA) Score			
IGA was an assessment scale used to determine severity of AD and clinical response to treatment on a 5-point scale (0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = severe) based on erythema and papulation/infiltration. Therapeutic response was an IGA score of 0 (clear) or 1 (almost clear).			
Units: Units on a scale arithmetic mean standard deviation	 4 ± 0.69	 3.9 ± 0.67	 -
Scoring Atopic Dermatitis (SCORAD) Score			
SCORAD is a clinical tool for assessing the severity of atopic dermatitis developed by the European Task Force on Atopic Dermatitis (Severity scoring of atopic dermatitis: the SCORAD index). Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology (Basel) 186 (1): 23–31. 1993. Extent and intensity of eczema as well as subjective signs (insomnia, etc.) are assessed and scored. Total score ranges from 0 (absent disease) to 103 (severe disease).			
Units: Units on a scale arithmetic mean standard deviation	 69.1 ± 13.38	 66.7 ± 13.82	 -
Body Surface Area (BSA)			
BSA affected by AD was assessed for each section of the body (the possible highest score for each region was: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs			

[36%], and genitals [1%]). It was reported as a percentage of all major body sections combined.			
Units: Percentage of BSA			
arithmetic mean	50.8	46.8	
standard deviation	± 24.13	± 24.55	-
5-D Pruritus Scale			
The 5-D Pruritus was a 5-question tool used in clinical trials to assess 5 dimensions of background itch: degree, duration, direction, disability, and distribution. Each question corresponded to 1 of the 5 dimensions of itch. Subjects rated their symptoms over the preceding 2-week period on a scale of 1 (least affected) to 5 (most affected).			
Units: Units on scale			
arithmetic mean	18.7	18.4	
standard deviation	± 3.5	± 3.04	-
Pruritus Numerical Rating Scale (NRS) Score			
Pruritus NRS scale is an assessment tool that is used to report the intensity of subject's pruritus (itch), both maximum and average intensity, during a 24-hour recall period. Subjects were asked the following question: how would a subject rate his itch at the worst moment during the previous 24 hours (for maximum itch intensity on a scale of 0 – 10 [0= no itch; 10= worst itch imaginable]).			
Units: units on a scale			
arithmetic mean	5.8	6.1	
standard deviation	± 1.93	± 1.34	-

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo (for Dupilumab) once weekly for 12 weeks.	
Reporting group title	Dupilumab 300 mg
Reporting group description:	
Dupilumab 300 mg once weekly for 12 weeks	

Primary: Percent Change From Baseline in Eczema Area and Severity Index (EASI) Score at Week 12- Last Observation Carried Forward (LOCF)

End point title	Percent Change From Baseline in Eczema Area and Severity Index (EASI) Score at Week 12- Last Observation Carried Forward (LOCF)[1]

End point description:

The EASI score was used to measure the severity and extent of AD and measured erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper and lower extremities. The total EASI score ranges from 0 (minimum) to 72 (maximum) points, with the higher scores reflecting the worse severity of AD. The efficacy data were set to be missing after use of rescue medication and after early termination visit for subjects who prematurely discontinued study treatment. Then, all missing values were imputed by simple LOCF. Full analysis set (FAS) population included all randomized subjects who received at least one dose of study drug and had at least 1 post-baseline efficacy assessment.

End point type	Primary

End point timeframe:

Baseline to 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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: percent change				
arithmetic mean (standard deviation)	-23.3 (± 49.26)	-74 (± 26.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Investigator’s Global Assessment (IGA) Score of "0" or "1" at Week 12- LOCF

End point title	Percentage of Subjects With Investigator’s Global Assessment (IGA) Score of "0" or "1" at Week 12- LOCF

End point description:

IGA is an assessment scale used to determine severity of AD and clinical response to treatment on a 5-

point scale (0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = severe) based on erythema and papulation/infiltration. Therapeutic response is an IGA score of 0 (clear) or 1 (almost clear). The efficacy data were set to be missing after use of rescue medication and after early termination visit for subjects who prematurely discontinued study treatment. Then, all missing values were imputed by simple LOCF. FAS population.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: Percentage of subjects				
number (not applicable)	7.4	40		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Who Achieved at Least a 50% Reduction from Baseline in the EASI Score (EASI 50) at Week 12- LOCF

End point title	Percentage of Subjects Who Achieved at Least a 50% Reduction from Baseline in the EASI Score (EASI 50) at Week 12- LOCF

End point description:

The EASI score was used to measure the severity and extent of AD and measured erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper and lower extremities. The total EASI score ranges from 0 (minimum) to 72 (maximum) points, with the higher scores reflecting the worse severity of AD. EASI-50 responders were the subjects who achieved ≥50% overall improvement in EASI score from baseline to Week 12. Efficacy data were set to be missing after use of rescue medication and after early termination visit for subjects who prematurely discontinued study treatment. Then, all missing values were imputed by simple LOCF. FAS population.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: Percentage of subjects				
number (not applicable)	35.2	85.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EASI Score at Week 12- LOCF

End point title	Change From Baseline in EASI Score at Week 12- LOCF

End point description:

The EASI score was used to measure the severity and extent of AD and measured erythema, infiltration, excoriation and lichenification on 4 anatomic regions of the body: head, trunk, upper and lower extremities. The total EASI score ranges from 0 (minimum) to 72 (maximum) points, with the higher scores reflecting the worse severity of AD. The efficacy data were set to be missing after use of rescue medication and after early termination visit for subjects who prematurely discontinued study treatment. Then, all missing values were imputed by simple LOCF. FAS population.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: Units on a scale				
arithmetic mean (standard deviation)	-6.4 (± 14.85)	-19.9 (± 11.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline in IGA Score at Week 12- LOCF

End point title	Percent Change From Baseline in IGA Score at Week 12- LOCF

End point description:

IGA is an assessment scale used to determine severity of AD and clinical response to treatment on a 5-point scale (0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = severe) based on erythema and papulation/infiltration. Therapeutic response is an IGA score of 0 (clear) or 1 (almost clear). The efficacy data were set to be missing after use of rescue medication and after early termination visit for subjects who prematurely discontinued study treatment. Then, all missing values were imputed by simple LOCF. FAS population.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: Percent Change				
arithmetic mean (standard deviation)	-14.7 (± 27.37)	-49.5 (± 25.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percent Body Surface Area (BSA) Affected by Atopic Dermatitis at Week 12- LOCF

End point title	Change From Baseline in Percent Body Surface Area (BSA) Affected by Atopic Dermatitis at Week 12- LOCF

End point description:

BSA affected by AD was assessed for each section of the body (the possible highest score for each region was: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], and genitals [1%]). It was reported as a percentage of all major body sections combined. The efficacy data were set to be missing after use of rescue medication and after early termination visit for subjects who prematurely discontinued study treatment. Then, all missing values were imputed by simple LOCF. FAS population.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: Percentage of BSA				
arithmetic mean (standard deviation)	-9 (± 21.07)	-27.4 (± 22.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Scoring Atopic Dermatitis (SCORAD) Score at Week 12- LOCF

End point title	Change From Baseline in Scoring Atopic Dermatitis (SCORAD) Score at Week 12- LOCF

End point description:

SCORAD is a clinical tool for assessing the severity of AD developed by the European Task Force on Atopic Dermatitis (Severity scoring of atopic dermatitis: the SCORAD index). Consensus Report of the European Task Force on Atopic Dermatitis. Dermatology (Basel) 186 (1): 23–31. 1993. Extent and intensity of eczema as well as subjective signs (insomnia, etc.) are assessed and scored. Total score ranges from 0 (absent disease) to 103 (severe disease). The efficacy data were set to be missing after use of rescue medication and after early termination visit for subjects who prematurely discontinued study treatment.Then, all missing values were imputed by simple LOCF.

End point type	Secondary

End point timeframe:
Baseline to Week 12

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: Units on a scale				
arithmetic mean (standard deviation)	-9.8 (± 20.53)	-35 (± 19.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pruritus Numerical Rating Scale (NRS) to Week 12- LOCF

End point title	Change From Baseline in Pruritus Numerical Rating Scale (NRS) to Week 12- LOCF

End point description:

Pruritus NRS was an assessment tool that was used to report the intensity of a subject's pruritus (itch), both maximum and average intensity, during a 24-hour recall period. Subjects were asked the following question: how would a subject rate his itch at the worst moment during the previous 24 hours (for maximum itch intensity on a scale of 0 – 10 [0 = no itch; 10 = worst itch imaginable]). The efficacy data were set to be missing after use of rescue medication and after early termination visit for subjects who prematurely discontinued study treatment. Then, all missing values were imputed by simple LOCF. FAS population. Number of subjects analyzed=subjects with available data for this endpoint.

End point type	Secondary

End point timeframe:
Baseline to Week 12

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	54		
Units: units on a scale				
arithmetic mean (standard deviation)	-0.9 (± 2.07)	-3.5 (± 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 5-D Pruritus Scale at Week 12

End point title	Change From Baseline in 5-D Pruritus Scale at Week 12

End point description:

The 5-D Pruritus Scale, was a 5-question tool used in clinical trials to assess 5 dimensions of background itch: degree, duration, direction, disability, and distribution. Each question corresponded to 1 of the 5 dimensions of itch. Subjects rated their symptoms over the preceding 2-week period on a scale of 1 (least affected) to 5 (most affected). FAS population.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	Dupilumab 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	55		
Units: units on a scale				
arithmetic mean (standard deviation)	-1.9 (± 4.28)	-7.4 (± 4.33)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Day 197) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events (AEs) are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (time from first dose of study drug through the end of study [Day 197]).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo (for Dupilumab) once weekly for 12 weeks by SC injection.

Reporting group title	Dupilumab 300 mg

Reporting group description:

Dupilumab 300 mg once weekly for 12 weeks by SC injection.

Serious adverse events	Placebo	Dupilumab 300 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 54 (12.96%)	1 / 55 (1.82%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 54 (0.00%)	1 / 55 (1.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			

subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	4 / 54 (7.41%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema herpeticum			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin bacterial infection			
subjects affected / exposed	1 / 54 (1.85%)	0 / 55 (0.00%)	
occurrences causally related to treatment / all	1 / 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	Dupilumab 300 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 54 (57.41%)	38 / 55 (69.09%)	
Investigations			
Neutrophil count increased			
subjects affected / exposed	3 / 54 (5.56%)	0 / 55 (0.00%)	
occurrences (all)	4	0	
White blood cell count increased			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	
occurrences (all)	4	1	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 54 (12.96%)	9 / 55 (16.36%)	
occurrences (all)	11	12	
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	3 / 54 (5.56%)	0 / 55 (0.00%)	
occurrences (all)	3	0	
Lymphadenopathy			
subjects affected / exposed	4 / 54 (7.41%)	0 / 55 (0.00%)	
occurrences (all)	4	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 54 (7.41%)	5 / 55 (9.09%)	
occurrences (all)	5	7	
Injection site erythema			
subjects affected / exposed	1 / 54 (1.85%)	4 / 55 (7.27%)	
occurrences (all)	1	7	
Injection site induration			
subjects affected / exposed	3 / 54 (5.56%)	5 / 55 (9.09%)	
occurrences (all)	3	6	
Injection site reaction			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	
occurrences (all)	1	6	
Eye disorders			
Conjunctivitis allergic			

subjects affected / exposed	0 / 54 (0.00%)	5 / 55 (9.09%)	
occurrences (all)	0	5	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 54 (7.41%)	1 / 55 (1.82%)	
occurrences (all)	7	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	4	
Oropharyngeal pain			
subjects affected / exposed	1 / 54 (1.85%)	3 / 55 (5.45%)	
occurrences (all)	1	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	3	
Infections and infestations			
Impetigo			
subjects affected / exposed	3 / 54 (5.56%)	1 / 55 (1.82%)	
occurrences (all)	3	1	
Conjunctivitis			
subjects affected / exposed	2 / 54 (3.70%)	8 / 55 (14.55%)	
occurrences (all)	2	11	
Nasopharyngitis			
subjects affected / exposed	10 / 54 (18.52%)	22 / 55 (40.00%)	
occurrences (all)	15	33	
Oral herpes			
subjects affected / exposed	0 / 54 (0.00%)	3 / 55 (5.45%)	
occurrences (all)	0	4	
Rhinitis			
subjects affected / exposed	2 / 54 (3.70%)	3 / 55 (5.45%)	
occurrences (all)	3	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 November 2011	Removed the SF-36 questionnaire from the protocol; Allowed the study drug to be administered in multiple SC locations, and split into 2 injections; Updated the AE severity grading to conform to the current safety template; Changed the end of study visit from week 18 (day 127) to week 20 (day 141); Added section for AEs of special interest; Added anti-parasitics and anti-protozoals to description of chronic or acute infection requiring treatment within 4 weeks of screening; Clarified that the efficacy analysis at week 12 was to be the primary efficacy analysis, not the final efficacy analysis; Revised pharmacokinetics sampling and analysis
12 March 2012	Clarified that the study was not limited to subjects with extrinsic AD; Corrected the definition of study drug stopping rules; Increased allowable screening and baseline EASI scores from 12 to 16; Added the collection of a Creatine Phosphokinase (CPK), Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Lactate Dehydrogenase (LDH) sample at days 8 and 22; Indicated that collection of the RNA sample (part of the research samples collected during the study) might require separate written informed consent, as required by local regulatory authorities; Clarified that each dose could be administered as a single 2 mL injection, or split into two 1 mL injections
20 August 2012	Increased the number of subjects in the study from 80 to 100; Extended the follow-up period from 8 weeks to 16 weeks (5 follow-up visits were added; overall study duration was extended from 20 weeks to 28 weeks); Increased the required use of adequate birth control measures following the last dose of study drug from 8 to 16 weeks

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/25006719