



Clinical trial results:

A multi-centre, single-blind, parallel group, clinical evaluation of the efficacy and safety of clindamycin 1% / benzoyl peroxide 3% and azelaic acid 20% in the topical treatment of mild to moderate acne vulgaris

Summary

EudraCT number	2013-004158-81
Trial protocol	Outside EU/EEA
Global end of trial date	08 September 2014

Results information

Result version number	v1 (current)
This version publication date	15 March 2016
First version publication date	14 March 2015

Trial information

Trial identification

Sponsor protocol code	200398
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	17 November 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare the efficacy and safety of a gel formulation containing a combination of clindamycin 10mg/g + benzoyl peroxide 30mg/g with a cream containing azelaic acid 20%.

Main Hypothesis to test:

- clindamycin 1% /benzoyl peroxide 3% is more effective than azelaic acid 20% in treating inflammatory acne lesions;
- clindamycin 1% /benzoyl peroxide 3% has faster speed of onset;
- clindamycin 1% /benzoyl peroxide 3% results in higher patient satisfaction
- Both treatment have an equal tolerability

Protection of trial subjects:

Duac and Skinoren administered according to SPC. Hence, no specific measures that were put in place to protect trial participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2014
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: 222
Worldwide total number of subjects	222
EEA total number of subjects	222

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)	106

Adults (18-64 years)	116
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Overall 222 participants (par.) with facial acne (vulgaris) were enrolled; of these, 111 par. were randomized in the combination treatment of 1.2% clindamycin phosphate (10mg/g) + 3% benzoyl peroxide [30mg/g]) (Duac) Arm and 110 par. in the 20% azelaic acid cream (Skinoren) Arm. A total of 217 randomized par. used study medication at least once.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor ^[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Duac

Arm description:

Participants topically applied a thin film of Duac gel once daily in the evening for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

Arm type	Experimental
Investigational medicinal product name	Duac
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Once daily in the evening. Duac 10mg/g + 30mg/g Gel contains 1% clindamycin and 3% BPO in a gel vehicle consisting of carbomer, dimethicone, disodium lauryl sulfosuccinate, edetate disodium, glycerol, colloidal hydrated silica, poloxamer, purified water, and sodium hydroxide

Arm title	Skinoren
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Arm description:

Participants topically applied a thin film of Skinoren cream twice daily (once in the morning and once in the evening) for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

Arm type	Active comparator
Investigational medicinal product name	Skinoren
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Twice daily in the morning and evening. Skinoren Creme contains 20% azelaic acid in a cream vehicle consisting of Arlatone 983S (polyoxyethylene fatty acid ester), cutina CBS (mixture of mono-diglycerides, fatty alcohols, triglycerides and wax esters), cetearyl octanoate, propylene glycol, glycerol 85% (E422), benzoic acid (E210), purified water.

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This is an evaluator-blinded study; therefore, participants, study center staff responsible for drug accountability and distribution, and other individuals involved with the conduct, analysis, and reporting of clinical study data were not blinded to study product allocations. The acne lesion assessor was unaware of which study product was being used (blinded).

Number of subjects in period 1^[2]	Duac	Skinoren
Started	108	109
Completed	104	102
Not completed	4	7
Not in Time Schedule	-	1
Consent withdrawn by subject	2	2
Non Compliance	1	-
The Visit Date was not in Timeline	-	1
Adverse event, non-fatal	1	-
Lost to follow-up	-	3

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Overall 222 participants (par.) with facial acne (vulgaris) were enrolled; of these, 111 par. were randomized in the combination treatment of 1.2% clindamycin phosphate (10mg/g) + 3% benzoyl peroxide [30mg/g]) (Duac) Arm and 110 par. in the 20% azelaic acid cream (Skinoren) Arm.

Baseline characteristics

Reporting groups

Reporting group title	Duac
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Reporting group description:

Participants topically applied a thin film of Duac gel once daily in the evening for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

Reporting group title	Skinoren
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Reporting group description:

Participants topically applied a thin film of Skinoren cream twice daily (once in the morning and once in the evening) for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

Reporting group values	Duac	Skinoren	Total
Number of subjects	108	109	217
Age categorical			
Units: Subjects			

Age continuous			
Participants presented include the Intent-to-Treat (ITT) Analysis Set, consisting of all randomized participants who used study medication at least once.			
Units: years			
arithmetic mean	20.1	20	
standard deviation	± 7.1	± 6.9	-
Gender categorical			
Participants presented include the Intent-to-Treat (ITT) Analysis Set, consisting of all randomized participants who used study medication at least once.			
Units: Subjects			
Female	47	51	98
Male	61	58	119
Race			
Participants presented include the Intent-to-Treat (ITT) Analysis Set, consisting of all randomized participants who used study medication at least once.			
Units: Subjects			
Asian	5	0	5
Caucasian	94	102	196
African	1	1	2
Other	8	6	14

End points

End points reporting groups

Reporting group title	Duac
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Reporting group description:

Participants topically applied a thin film of Duac gel once daily in the evening for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

Reporting group title	Skinoren
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Reporting group description:

Participants topically applied a thin film of Skinoren cream twice daily (once in the morning and once in the evening) for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

Primary: Percent change from Baseline in inflammatory lesion counts at Week 4

End point title	Percent change from Baseline in inflammatory lesion counts at Week 4
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End point description:

Lesions were counted confined to the face; inflammatory lesions (ILs) (considering nasal lesions) included papules and pustules. A papule is a small, raised, red, dome-shaped palpable lesion while a pustule is a raised, dome-shaped palpable lesion containing yellow fluid (pus). Percent change from Baseline was calculated as the value at Week 4 minus the value at Baseline (Day 1) divided by the Baseline value*100. The Modified Intent-to-Treat (mITT) Analysis Set included all participants in the ITT Analysis Set who had a Baseline measurement of the number of ILs and who had at least one post-Baseline measurement of the number of ILs.

End point type	Primary
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End point timeframe:

Baseline and Week 4

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[1]	108 ^[2]		
Units: Percent change in lesions				
arithmetic mean (standard deviation)	-51.9 (± 27.6)	-38.1 (± 30.9)		

Notes:

[1] - mITT Analysis Set

[2] - mITT Analysis Set

Statistical analyses

Statistical analysis title	Analysis 1
Comparison groups	Skinoren v Duac

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004 ^[3]
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - Two-sided Mann-Whitney U-test for independent samples - normal approximation

Secondary: Absolute change from Baseline in ILs, NILs and total lesion count at Weeks 2, 4, 8 and 12

End point title	Absolute change from Baseline in ILs, NILs and total lesion count at Weeks 2, 4, 8 and 12
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End point description:

Lesions were counted confined to the face; ILs (considering nasal lesions) included papules and pustules. NILs included open comedones and closed comedones. An open comedo is an open, widely dilated follicle with black-coloured sebum, due to melanin and oxidation, and keratinous material that forms a plug, thereby obstructing the pilosebaceous duct. A closed comedo is a closed follicle filled with impacted sebum covered by keratin that has a whitish color. A papule is a small, raised, red, dome-shaped palpable lesion while a pustule is a raised, dome-shaped palpable lesion containing yellow fluid (pus). The total lesion (TLs) count was calculated as the sum of ILs and NILs. Change from Baseline was calculated as the values at Weeks 2,4,8 and 12 minus the value at Baseline (Day 1).

End point type	Secondary
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End point timeframe:

Baseline and Weeks 2, 4, 8 and 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[4]	108 ^[5]		
Units: Absolute change in lesions				
arithmetic mean (standard deviation)				
IL, Week 2, n=105,108	-10.3 (± 8.3)	-6.3 (± 7.8)		
IL, Week 4, n=105,107	-14.2 (± 9.1)	-9.7 (± 8.6)		
IL, Week 8, n=104,102	-17.7 (± 9.7)	-12.7 (± 8.6)		
IL, Week 12 or early withdrawal, n=107,104	-19.6 (± 10.1)	-14.2 (± 8.9)		
NIL, Week 2, n=105,108	-13.7 (± 19)	-8.5 (± 13.3)		
NIL, Week 4, n=105,107	-21.2 (± 21.5)	-16 (± 19.1)		
NIL, Week 8, n=104,102	-26.8 (± 27.1)	-20.9 (± 23.6)		
NIL, Week 12 or early withdrawal, n=107,104	-32 (± 27.2)	-23.3 (± 24.9)		
TL, Week 2, n=105,108	-23.9 (± 22.3)	-14.8 (± 16.7)		
TL, Week 4, n=105,107	-35.4 (± 25)	-25.7 (± 22.3)		
TL, Week 8, n=104,102	-44.4 (± 31.3)	-33.6 (± 27.5)		
TL, Week 12 or early withdrawal, n=107,104	-51.6 (± 30.9)	-37.5 (± 29)		

Notes:

[4] - mITT Analysis Set

[5] - mITT Analysis Set

Statistical analyses

Secondary: Percent change from Baseline in ILs, NILs and total lesion count at Weeks 2, 4, 8 and 12

End point title	Percent change from Baseline in ILs, NILs and total lesion count at Weeks 2, 4, 8 and 12
End point description:	
Lesions were counted confined to the face; ILs (considering nasal lesions) included papules and pustules. NILs included open comedones and closed comedones. An open comedo is an open, widely dilated follicle with black-coloured sebum, due to melanin and oxidation, and keratinous material that forms a plug, thereby obstructing the pilosebaceous duct. A closed comedo is a closed follicle filled with impacted sebum covered by keratin that has a whitish color. A papule is a small, raised, red, dome-shaped palpable lesion while a pustule is a raised, dome-shaped palpable lesion containing yellow fluid (pus). The total lesion count was calculated as the sum of ILs and NILs. Percent change from Baseline was calculated as the values at Weeks 2,4,8 and 12 minus the value at Baseline (Day 1) divided by Baseline value*100.	
End point type	Secondary
End point timeframe:	
Baseline and Weeks 2, 4, 8 and 12	

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[6]	108 ^[7]		
Units: Percent change in lesions				
arithmetic mean (standard deviation)				
IL, Week 2, n=105,108	-37.3 (± 27.7)	-24.2 (± 30.3)		
IL, Week 8, n=104,102	-65 (± 26.3)	-49.1 (± 30.9)		
IL, Week 12 or early withdrawal, n=107,104	-72.3 (± 25)	-55 (± 29.8)		
NIL, Week 2, n=105,108	-23.5 (± 25.3)	-14.9 (± 23.4)		
NIL, Week 4, n=105,107	-38.1 (± 27.8)	-27 (± 28.2)		
NIL, Week 8, n=104,102	-48.5 (± 39.8)	-35.5 (± 31.2)		
NIL, Week 12 or early withdrawal, n=107,104	-60.6 (± 35.3)	-42.1 (± 37.5)		
TL, Week 2, n=105,108	-28.7 (± 22.3)	-18.4 (± 20.3)		
TL, Week 4, n=105,107	-43.8 (± 23.3)	-30.8 (± 23)		
TL, Week 8, n=104,102	-55.2 (± 30.5)	-40.1 (± 27.4)		
TL, Week 12 or early withdrawal, n=107,104	-64.6 (± 26.9)	-46.1 (± 31.8)		

Notes:

[6] - mITT Analysis Set

[7] - mITT Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Shift change from Baseline in total lesions count by the Investigator's Static Global Assessment (ISGA) at Weeks 2, 4, 8 and 12

End point title	Shift change from Baseline in total lesions count by the Investigator's Static Global Assessment (ISGA) at Weeks 2, 4, 8 and 12
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End point description:

Investigator evaluated the acne severity (S) of the participant's face using the ISGA scale, ranging from 0 to 5: 0=clear skin with no ILs or NILs; 1=almost clear: rare NIL with no more than one small ILs; 2=mild S: >G 1, some NILs with no more than a few ILs (papules/ pustules only, no nodular lesions [NLs]); 3=moderate S: >G 2, up to many NILs and may have some ILs, but no more than one small NL; 4=severe: greater than G 3, up to many NILs and ILs, but no more than a few NLs; 5=very severe: many NILs and ILs and more than a few NLs, may have cystic lesions. A shift table was provided to deduce how the number of participants were varying from the Baseline visit to the post-Baseline visits. Week 12 represents Week 12 or early withdrawal.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 2, 4, 8 and 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[8]	108 ^[9]		
Units: Participants				
Mild (Baseline) to Almost clear (Week 2)	4	1		
Mild (Baseline) to Mild (Week 2)	27	28		
Mild (Baseline) to Moderate (Week 2)	3	8		
Moderate (Baseline) to Almost Clear (Week 2)	1	1		
Moderate (Baseline) to Mild (Week 2)	26	14		
Moderate (Baseline) to Moderate (Week 2)	44	56		
Moderate (Baseline) to Missing (Week 2)	2	0		
Mild (Baseline) to Almost clear (Week 4)	8	8		
Mild (Baseline) to Mild (Week 4)	25	24		
Mild (Baseline) to Moderate (Week 4)	1	4		
Mild (Baseline) to Missing (Week 4)	0	1		
Moderate (Baseline) to Almost Clear (Week 4)	11	3		
Moderate (Baseline) to Mild (Week 4)	29	24		
Moderate (Baseline) to Moderate (Week 4)	31	43		
Moderate (Baseline) to Severe (Week 4)	0	1		
Moderate (Baseline) to Missing (Week 4)	2	1		
Mild (Baseline) to Clear (Week 8)	2	0		
Mild (Baseline) to Almost Clear (Week 8)	10	10		
Mild (Baseline) to Mild (Week 8)	19	15		
Mild (Baseline) to Moderate (Week 8)	3	8		
Mild (Baseline) to Missing (Week 8)	0	4		
Moderate (Baseline) to Clear (Week 8)	1	0		
Moderate (Baseline) to Almost Clear (Week 8)	15	5		
Moderate (Baseline) to Mild (Week 8)	32	27		
Moderate (Baseline) to Moderate (Week 8)	22	37		
Moderate (Baseline) to Missing (Week 8)	3	2		
Mild (Baseline) to Clear (Week 12)	3	1		
Mild (Baseline) to Almost Clear (Week 12)	12	9		

Mild (Baseline) to Mild (Week 12)	17	17		
Mild (Baseline) to Moderate (Week 12)	2	8		
Mild (Baseline) to Missing (Week 12)	0	2		
Moderate (Baseline) to Clear (Week 12)	2	0		
Moderate (Baseline) to Almost Clear (Week 12)	19	9		
Moderate (Baseline) to Mild (Week 12)	33	26		
Moderate (Baseline) to Moderate (Week 12)	19	32		
Moderate (Baseline) to Severe (Week 12)	0	2		
Moderate (Baseline) to Missing (Week 12)	0	2		

Notes:

[8] - mITT Analysis Set

[9] - mITT Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Time from Baseline to a 50% reduction in TL count

End point title	Time from Baseline to a 50% reduction in TL count
End point description:	
Time to a 50% reduction in TL count (sum of ILs and NILs) was the time difference between Baseline and the time to a 50% reduction in LC.	
End point type	Secondary
End point timeframe:	
From Baseline up to Week 12	

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91 ^[10]	60 ^[11]		
Units: Days				
median (full range (min-max))	52 (11 to 104)	55 (12 to 97)		

Notes:

[10] - mITT Analysis Set. Only those participants with a 50% reduction were included in this analysis.

[11] - mITT Analysis Set. Only those participants with a 50% reduction were included in this analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reported for the indicated Subject's Global Change Assessment (SGCA) category at Weeks 2, 4, 8 and 12

End point title	Number of participants reported for the indicated Subject's Global Change Assessment (SGCA) category at Weeks 2, 4, 8 and 12
End point description:	
Participant reported change in the following categories: "very much improved, much improved, minimally improved, no change, minimally worse, much worse and very much worse". Week 12 represents Week 12 or early withdrawal.	

End point type	Secondary
End point timeframe:	
Weeks 2, 4, 8 and 12	

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[12]	108 ^[13]		
Units: Participants				
Week 2, Very Much Improved	4	2		
Week 4, Very Much Improved	5	0		
Week 8, Very Much Improved	9	1		
Week 12, Very Much Improved	14	8		
Week 2, Much Improved	51	30		
Week 4, Much Improved	48	39		
Week 8, Much Improved	54	44		
Week 12, Much Improved	48	38		
Week 2, Minimally Improved	44	56		
Week 4, Minimally Improved	44	49		
Week 8, Minimally Improved	30	32		
Week 12, Minimally Improved	29	33		
Week 2, No change	6	14		
Week 4, No change	2	12		
Week 8, No change	7	15		
Week 12, No change	10	17		
Week 2, Minimally Worse	0	6		
Week 4, Minimally Worse	6	7		
Week 8, Minimally Worse	3	8		
Week 12, Minimally Worse	4	5		
Week 2, Much Worse	0	0		
Week 4, Much Worse	0	0		
Week 8, Much Worse	1	1		
Week 12, Much Worse	0	2		
Week 2, Very Much Worse	0	0		
Week 4, Very Much Worse	0	0		
Week 8, Very Much Worse	0	1		
Week 12, Very Much Worse	2	1		
Week 2, Missing	2	0		
Week 4, Missing	2	1		
Week 8, Missing	3	6		
Week 12, Missing	0	4		

Notes:

[12] - mITT Analysis Set

[13] - mITT Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with a shift change from Baseline for erythema,

peeling and dryness at Weeks 2, 4, 8 and 12, as assessed by the Investigator

End point title	Number of participants with a shift change from Baseline for erythema, peeling and dryness at Weeks 2, 4, 8 and 12, as assessed by the Investigator
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End point description:

Erythema (Er) is a skin condition characterized by redness or rash; peeling (Pl) skin is damage to and loss of the upper layer of skin; and dry skin (dry) is an uncomfortable condition marked by scaling, itching, and cracking. Local tolerability assessments were performed by the Investigator at each study visit and were graded based on severity as 0 to 3: 0=none; 1=slight; 2=some (erythema and dry skin)/moderate(peeling); 3=very red (erythema)/very dry (dry skin)/strong (peeling). Week 12 represents Week 12 or early withdrawal.

End point type	Secondary
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End point timeframe:

Weeks 2, 4 ,8 and 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[14]	108 ^[15]		
Units: Participants				
Er, None (Baseline) to None (Week 2)	39	33		
Er, None (Baseline) to Slight (Week 2)	11	18		
Er, None (Baseline) to Some (Week 2)	0	1		
Er, None (Baseline) to Missing (Week 2)	1	0		
Er, None (Baseline) to None (Week 4)	40	36		
Er, None (Baseline) to Slight (Week 4)	9	13		
Er, None (Baseline) to Some (Week 4)	1	3		
Er, None (Baseline) to Missing (Week 4)	1	0		
Er, None (Baseline) to None (Week 8)	40	29		
Er, None (Baseline) to Slight (Week 8)	10	19		
Er, None (Baseline) to Some (Week 8)	0	2		
Er, None (Baseline) to Missing (Week 8)	1	2		
Er, None (Baseline) to None (Week 12)	45	32		
Er, None (Baseline) to Slight (Week 12)	6	18		
Er, None (Baseline) to Missing (Week 12)	0	2		
Er, Slight (Baseline) to None (Week 2)	12	12		
Er, Slight (Baseline) to Slight (Week 2)	19	18		
Er, Slight (Baseline) to Some (Week 2)	1	8		
Er, Slight (Baseline) to Missing (Week 2)	1	0		
Er, Slight (Baseline)to None (Week 4)	18	19		
Er, Slight (Baseline) to Slight (Week 4)	11	17		
Er, Slight (Baseline) to Some (Week 4)	3	1		
Er, Slight (Baseline) to Missing (Week 4)	1	1		
Er, Slight (Baseline) to None (Week 8)	15	17		
Er, Slight (Baseline) to Slight (Week 8)	11	17		
Er, Slight (Baseline) to Some (Week 8)	5	1		
Er, Slight (Baseline) to Missing (Week 8)	2	3		
Er, Slight (Baseline) to None (Week 12)	21	22		
Er, Slight (Baseline) to Slight (Week 12)	11	13		
Er, Slight (Baseline) to Some (Week 12)	0	2		

Er, Slight (Baseline) to Very red (Week 12)	1	0		
Er, Slight (Baseline) to Missing (Week 12)	0	1		
Er, Some (Baseline) to None (Week 2)	3	1		
Er, Some (Baseline) to Slight (Week 2)	10	11		
Er, Some (Baseline) to Some (Week 2)	6	3		
Er, Some (Baseline) to None (Week 4)	5	3		
Er, Some (Baseline) to Slight (Week 4)	11	9		
Er, Some (Baseline) to Some (Week 4)	3	2		
Er, Some (Baseline) to Missing (Week 4)	0	1		
Er, Some (Baseline) to None (Week 8)	8	1		
Er, Some (Baseline) to Slight (Week 8)	9	12		
Er, Some (Baseline) to Some (Week 8)	1	1		
Er, Some (Baseline) to Very red (Week 8)	1	0		
Er, Some (Baseline) to Missing (Week 8)	0	1		
Er, Some (Baseline) to None (Week 12)	9	4		
Er, Some (Baseline) to Slight (Week 12)	8	9		
Er, Some (Baseline) to Some (Week 12)	2	1		
Er, Some (Baseline) to Missing (Week 12)	0	1		
Er, Very red (Baseline) to Slight (Week 2)	1	1		
Er, Very red (Baseline) to Some (Week 2)	2	2		
Er, Very red (Baseline) to Slight (Week 4)	2	2		
Er, Very red (Baseline) to Some (Week 4)	1	1		
Er, Very red (Baseline) to None (Week 8)	2	0		
Er, Very red (Baseline) to Slight (Week 8)	1	3		
Er, Very red (Baseline) to None (Week 12)	0	2		
Er, Very red (Baseline) to Slight (Week 12)	1	1		
Er, Very red (Baseline) to Some (Week 12)	2	0		
Pl, None (Baseline) to None (Week 2)	65	73		
Pl, None (Baseline) to Slight (Week 2)	13	11		
Pl, None (Baseline) to Moderate (Week 2)	1	0		
Pl, None (Baseline) to Missing (Week 2)	2	0		
Pl, None (Baseline) to None (Week 4)	70	72		
Pl, None (Baseline) to Slight (Week 4)	9	11		
Pl, None (Baseline) to Missing (Week 4)	2	1		
Pl, None (Baseline) to None (Week 8)	69	69		
Pl, None (Baseline) to Slight (Week 8)	9	10		
Pl, None (Baseline) to Missing (Week 8)	3	5		
Pl, None (Baseline) to None (Week 12)	74	70		
Pl, None (Baseline) to Slight (Week 12)	7	11		
Pl, None (Baseline) to Missing (Week 12)	0	3		
Pl, Slight (Baseline) to None (Week 2)	8	8		
Pl, Slight (Baseline) to Slight (Week 2)	10	13		

PI, Slight (Baseline) to Moderate (Week 2)	3	2		
PI, Slight (Baseline) to None (Week 4)	15	13		
PI, Slight (Baseline) to Slight (Week 4)	5	9		
PI, Slight (Baseline) to Moderate (Week 4)	1	1		
PI, Slight (Baseline) to None (Week 8)	18	12		
PI, Slight (Baseline) to Slight (Week 8)	3	10		
PI, Slight (Baseline) to Missing (Week 8)	0	1		
PI, Slight (Baseline) to None (Week 12)	14	15		
PI, Slight (Baseline) to Slight (Week 12)	7	7		
PI, Slight (Baseline) to Missing (Week 12)	0	1		
PI, Moderate (Baseline) to None (Week 2)	2	0		
PI, Moderate (Baseline) to Slight (Week 2)	2	1		
PI, Moderate (Baseline) to None (Week 4)	2	1		
PI, Moderate (Baseline) to Slight (Week 4)	1	0		
PI, Moderate (Baseline) to Moderate (Week 4)	1	0		
PI, Moderate (Baseline) to None (Week 8)	3	1		
PI, Moderate (Baseline) to Slight (Week 8)	1	0		
PI, Moderate (Baseline) to None (Week 12)	2	0		
PI, Moderate (Baseline) to Slight (Week 12)	2	1		
Dry, None (Baseline) to None (Week 2)	55	65		
Dry, None (Baseline) to Slight (Week 2)	14	9		
Dry, None (Baseline) to Some (Week 2)	1	3		
Dry, None (Baseline) to Missing (Week 2)	2	0		
Dry, None (Baseline) to None (Week 4)	61	64		
Dry, None (Baseline) to Slight (Week 4)	9	12		
Dry, None (Baseline) to Missing (Week 4)	2	1		
Dry, None (Baseline) to None (Week 8)	61	61		
Dry, None (Baseline) to Slight (Week 8)	8	11		
Dry, None (Baseline) to Missing (Week 8)	3	5		
Dry, None (Baseline) to None (Week 12)	69	66		
Dry, None (Baseline) to Slight (Week 12)	2	8		
Dry, None (Baseline) to Some (Week 12)	1	0		
Dry, None (Baseline) to Missing (Week 12)	0	3		
Dry, Slight (Baseline) to None (Week 2)	11	7		
Dry, Slight (Baseline) to Slight (Week 2)	11	12		
Dry, Slight (Baseline) to Some (Week 2)	3	6		
Dry, Slight (Baseline) to None (Week 4)	14	10		
Dry, Slight (Baseline) to Slight (Week 4)	9	12		
Dry, Slight (Baseline) to Some (Week 4)	2	3		
Dry, Slight (Baseline) to None (Week 8)	19	12		

Dry, Slight (Baseline) to Slight (Week 8)	6	11		
Dry, Slight (Baseline) to Some (Week 8)	0	1		
Dry, Slight (Baseline) to Missing (Week 8)	0	1		
Dry, Slight (Baseline) to None (Week 12)	14	15		
Dry, Slight (Baseline) to Slight (Week 12)	11	8		
Dry, Slight (Baseline) to Some (Week 12)	0	1		
Dry, Slight (Baseline) to Missing (Week 12)	0	1		
Dry, Some (Baseline) to None (Week 2)	4	2		
Dry, Some (Baseline) to Slight (Week 2)	1	2		
Dry, Some (Baseline) to Some (Week 2)	4	2		
Dry, Some (Baseline) to None (Week 4)	4	1		
Dry, Some (Baseline) to Slight (Week 4)	3	5		
Dry, Some (Baseline) to Some (Week 4)	2	0		
Dry, Some (Baseline) to None (Week 8)	5	1		
Dry, Some (Baseline) to Slight (Week 8)	4	5		
Dry, Some (Baseline) to None (Week 12)	6	3		
Dry, Some (Baseline) to Slight (Week 12)	3	3		

Notes:

[14] - mITT Analysis Set

[15] - mITT Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with a shift change from Baseline for pruritis and burning/stinging at Weeks 2, 4, 8 and 12

End point title	Number of participants with a shift change from Baseline for pruritis and burning/stinging at Weeks 2, 4, 8 and 12
-----------------	--

End point description:

Itching or pruritis (Pr) is a sensation that causes the desire or reflex to scratch; burning/stinging (St/Bn) is a pain and burning sensation. Local tolerability assessments for burning/stinging and itching were performed by the participant and were graded based on severity as 0 to 3. 0=none; 1=slight; 2=moderate; 3=strong. Week 12 represents Week 12 or early withdrawal.

End point type	Secondary
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End point timeframe:

Weeks 2, 4 ,8 and 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[16]	108 ^[17]		
Units: Participants				
St/Bn, None (Baseline) to None (Week 2)	63	42		

St/Bn, None (Baseline) to Slight (Week 2)	14	23		
St/Bn, None (Baseline) to Moderate (Week 2)	4	8		
St/Bn, None (Baseline) to Strong (Week 2)	1	4		
St/Bn, None (Baseline) to Missing (Week 2)	2	0		
St/Bn, None (Baseline) to None (Week 4)	70	41		
St/Bn, None (Baseline) to Slight (Week 4)	11	29		
St/Bn, None (Baseline) to Moderate (Week 4)	1	6		
St/Bn, None (Baseline) to Missing (Week 4)	2	1		
St/Bn, None (Baseline) to None (Week 8)	75	46		
St/Bn, None (Baseline) to Slight (Week 8)	5	21		
St/Bn, None (Baseline) to Moderate (Week 8)	1	4		
St/Bn, None (Baseline) to Strong (Week 8)	0	1		
St/Bn, None (Baseline) to Missing (Week 8)	3	5		
St/Bn, None (Baseline) to None (Week 12)	75	47		
St/Bn, None (Baseline) to Slight (Week 12)	6	19		
St/Bn, None (Baseline) to Moderate (Week 12)	1	5		
St/Bn, None (Baseline) to Strong (Week 12)	1	2		
St/Bn, None (Baseline) to Missing (Week 12)	1	4		
St/Bn, Slight (Baseline) to None (Week 2)	14	10		
St/Bn, Slight (Baseline) to Slight (Week 2)	4	10		
St/Bn, Slight (Baseline) to Moderate (Week 2)	3	2		
St/Bn, Slight (Baseline) to Strong (Week 2)	0	2		
St/Bn, Slight (Baseline) to None (Week 4)	12	9		
St/Bn, Slight (Baseline) to Slight (Week 4)	8	13		
St/Bn, Slight (Baseline) to Moderate (Week 4)	1	1		
St/Bn, Slight (Baseline) to Strong (Week 4)	0	1		
St/Bn, Slight (Baseline) to None (Week 8)	18	10		
St/Bn, Slight (Baseline) to Slight (Week 8)	2	12		
St/Bn, Slight (Baseline) to Moderate (Week 8)	1	1		
St/Bn, Slight (Baseline) to Strong (Week 8)	0	1		
St/Bn, Slight (Baseline) to None (Week 12)	18	9		

St/Bn, Slight (Baseline) to Slight (Week 12)	3	11		
St/Bn, Slight (Baseline) to Moderate (Week 12)	0	3		
St/Bn, Slight (Baseline) to Strong (Week 12)	0	1		
St/Bn, Moderate (Baseline) to None (Week 2)	0	1		
St/Bn, Moderate (Baseline) to Slight (Week 2)	1	3		
St/Bn, Moderate (Baseline) to Moderate (Week 2)	0	2		
St/Bn, Moderate (Baseline) to None (Week 4)	0	2		
St/Bn, Moderate (Baseline) to Slight (Week 4)	1	3		
St/Bn, Moderate (Baseline) to Strong (Week 4)	0	1		
St/Bn, Moderate (Baseline) to None (Week 8)	0	1		
St/Bn, Moderate (Baseline) to Slight (Week 8)	1	2		
St/Bn, Moderate (Baseline) to Moderate (Week 8)	0	2		
St/Bn, Moderate (Baseline) to Missing (Week 8)	0	1		
St/Bn, Moderate (Baseline) to None (Week 12)	1	2		
St/Bn, Moderate (Baseline) to Slight (Week 12)	0	3		
St/Bn, Moderate (Baseline) to Moderate (Week 12)	0	1		
St/Bn, Strong (Baseline) to None (Week 2)	0	1		
St/Bn, Strong (Baseline) to None (Week 4)	0	1		
St/Bn, Strong (Baseline) to None (Week 8)	0	1		
St/Bn, Strong (Baseline) to Slight (Week 12)	0	1		
Pr, None (Baseline) to None (Week 2)	43	28		
Pr, None (Baseline) to Slight (Week 2)	14	27		
Pr, None (Baseline) to Moderate (Week 2)	4	7		
Pr, None (Baseline) to Strong (Week 2)	0	1		
Pr, None (Baseline) to Missing (Week 2)	2	0		
Pr, None (Baseline) to None (Week 4)	45	27		
Pr, None (Baseline) to Slight (Week 4)	14	30		
Pr, None (Baseline) to Moderate (Week 4)	2	5		
Pr, None (Baseline) to Missing (Week 4)	2	1		
Pr, None (Baseline) to None (Week 8)	47	33		
Pr, None (Baseline) to Slight (Week 8)	13	26		
Pr, None (Baseline) to Strong (Week 8)	0	1		
Pr, None (Baseline) to Missing (Week 8)	3	3		
Pr, None (Baseline) to None (Week 12)	51	33		
Pr, None (Baseline) to Slight (Week 12)	11	22		
Pr, None (Baseline) to Moderate (Week 12)	1	3		

Pr, None (Baseline) to Strong (Week 12)	0	1		
Pr, None (Baseline) to Missing (Week 12)	0	4		
Pr, Slight (Baseline) to None (Week 2)	13	10		
Pr, Slight (Baseline) to Slight (Week 2)	20	15		
Pr, Slight (Baseline) to Moderate (Week 2)	5	9		
Pr, Slight (Baseline) to Strong (Week 2)	1	4		
Pr, Slight (Baseline) to None (Week 4)	17	12		
Pr, Slight (Baseline) to Slight (Week 4)	20	19		
Pr, Slight (Baseline) to Moderate (Week 4)	2	6		
Pr, Slight (Baseline) to Strong (Week 4)	0	1		
Pr, Slight (Baseline) to None (Week 8)	21	11		
Pr, Slight (Baseline) to Slight (Week 8)	14	18		
Pr, Slight (Baseline) to Moderate (Week 8)	4	4		
Pr, Slight (Baseline) to Strong (Week 8)	0	2		
Pr, Slight (Baseline) to Missing (Week 8)	0	3		
Pr, Slight (Baseline) to None (Week 12)	22	11		
Pr, Slight (Baseline) to Slight (Week 12)	15	19		
Pr, Slight (Baseline) to Moderate (Week 12)	2	6		
Slight (Baseline) to Strong (Week 12)	0	2		
Pr, Moderate (Baseline) to None (Week 2)	2	4		
Pr, Moderate (Baseline) to Slight (Week 2)	1	1		
Pr, Moderate (Baseline) to Moderate (Week 2)	1	0		
Pr, Moderate (Baseline) to None (Week 4)	2	2		
Pr, Moderate (Baseline) to Slight (Week 4)	2	2		
Pr, Moderate (Baseline) to Moderate (Week 4)	0	1		
Pr, Moderate (Baseline) to None (Week 8)	3	2		
Pr, Moderate (Baseline) to Slight (Week 8)	1	3		
Pr, Moderate (Baseline) to None (Week 12)	3	1		
Pr, Moderate (Baseline) to Slight (Week 12)	1	4		
Pr, Strong (Baseline) to Strong (Week 2)	0	2		
Pr, Strong (Baseline) to Strong (Week 4)	0	2		
Pr, Strong (Baseline) to Moderate (Week 8)	0	1		
Pr, Strong (Baseline) to Strong (Week 8)	0	1		
Pr, Strong (Baseline) to Slight (Week 12)	0	1		
Pr, Strong (Baseline) to Strong (Week 12)	0	1		

Notes:

[16] - mITT Analysis Set

[17] - mITT Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in the Children's Dermatology Life Quality Index (CDLQI) score from Baseline at Weeks 2, 4, 8 and 12 in participants 12 to 16 years of age

End point title	Absolute change in the Children's Dermatology Life Quality Index (CDLQI) score from Baseline at Weeks 2, 4, 8 and 12 in participants 12 to 16 years of age
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End point description:

The CDLQI was used in children 12 to 16 years of age. The CDLQI was used to measure how much the participant's skin problem had affected their life over the last week. The CDLQI total score ranges from 0 to 30 where 0-1=no effect at all on the participant's life; 2-6=small effect on the participant's life; 7-12=moderate effect on the participant's life; 13-18=very large effect on the participant's life; 19-30=extremely large effect on the participant's life. The higher the score, the more quality of life was impaired. Absolute change from Baseline was calculated as the values at Weeks 2, 4, 8 and 12 minus the value at Baseline (Day 1).

End point type	Secondary
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End point timeframe:

Baseline, Weeks 2, 4, 8 and 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45 ^[18]	47 ^[19]		
Units: Absolute change of total score				
arithmetic mean (standard deviation)				
Week 2, n=38,42	-2.61 (± 2.89)	-1.31 (± 2.29)		
Week 4; n=38,42	-2.55 (± 2.41)	-1.55 (± 2.01)		
Week 8, n=38,42	-2.68 (± 2.76)	-1.67 (± 2.34)		
Week 12 or early withdrawal, n=38,42	-2.87 (± 2.75)	-1.55 (± 2.56)		

Notes:

[18] - mITT Analysis Set. Only those participants 12 to 16 years of age were included in the analysis.

[19] - mITT Analysis Set. Only those participants 12 to 16 years of age were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change in the Dermatology Life Quality Index (DLQI) score from Baseline at Weeks 2, 4, 8 and 12 in participants 17 years of age or older

End point title	Absolute change in the Dermatology Life Quality Index (DLQI) score from Baseline at Weeks 2, 4, 8 and 12 in participants 17 years of age or older
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End point description:

The DLQI was used in participants 17 years of age or older. The DLQI was used to measure how much the participant's skin problem had affected their life over the last week. The DLQI total score ranges from 0 to 30 where 0-1=no effect at all on the participant's life; 2-5=small effect on the participant's life; 6-10=moderate effect on the participant's life; 11-20=very large effect on the participant's life; 21-30=extremely large effect on the participant's life. The higher the score, the more quality of life was impaired. Absolute change from Baseline was calculated as the values at Weeks 2, 4, 8 and 12 minus the value at Baseline (Day 1).

End point type	Secondary
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End point timeframe:

Baseline, Weeks 2, 4, 8 and 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	62 ^[20]	61 ^[21]		
Units: Absolute change of total score				
arithmetic mean (standard deviation)				
Week 2, n=54,53	-2.28 (± 2.81)	-2.17 (± 3.72)		
Week 4, n=56,52	-3.39 (± 3.33)	-3.15 (± 3.52)		
Week 8, n=55,50	-4.04 (± 3.7)	-3.38 (± 4.6)		
Week 12 or early withdrawal, n=57,51	-4.46 (± 3.8)	-3.12 (± 4.94)		

Notes:

[20] - mITT Analysis Set. Only those participants 17 years or older were included in the analysis.

[21] - mITT Analysis Set. Only those participants 17 years or older were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the overall satisfaction score at Week 12, rated using the Product Acceptability and Preference Questionnaire

End point title	Number of participants with the overall satisfaction score at Week 12, rated using the Product Acceptability and Preference Questionnaire
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End point description:

The Product Acceptability and Preference Questionnaire was completed by the participant at Week 12. The participant rated their overall satisfaction using the following scale: 1-very satisfied; 2- satisfied; 3- neutral; 4-unsatisfied; 5-very unsatisfied.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[22]	108 ^[23]		
Units: Participants				
Very satisfied	41	26		
Satisfied	61	43		
Neutral	4	21		

Unsatisfied	1	11		
Very unsatisfied	0	3		

Notes:

[22] - mITT Analysis Set

[23] - mITT Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the number of missed applications of treatment medication from Baseline to Week 12

End point title	Number of participants with the number of missed applications of treatment medication from Baseline to Week 12
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End point description:

Number of participants with the number of missed applications of treatment medication from Baseline to Week 12 was analyzed.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107 ^[24]	108 ^[25]		
Units: Participants				
0 missed application	51	38		
1 missed application	21	8		
2 missed application	12	4		
3 missed application	4	4		
4 missed application	4	5		
5 missed application	1	5		
6 missed application	3	7		
7 missed application	2	6		
8 missed application	1	3		
9 missed application	1	5		
10 missed application	1	2		
11 missed application	1	3		
12 missed application	0	1		
13 missed application	1	2		
14 missed application	1	5		
16 missed application	1	0		
17 missed application	1	1		
18 missed application	1	1		
19 missed application	0	1		
21 missed application	0	2		
22 missed application	0	1		
23 missed application	0	1		
31 missed application	0	1		
39 missed application	0	1		

Missing	0	1		
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Notes:

[24] - mITT Analysis Set

[25] - mITT Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) or serious adverse event (SAE)

End point title	Number of participants with any adverse event (AE) or serious adverse event (SAE)
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End point description:

AE is defined as any untoward medical occurrence in a participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. A SAE is defined as any untoward medical occurrence that, at any dose: results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability or incapacity, or is a congenital anomaly or birth defect. Medical or scientific judgment should be exercised in other situations. Refer to the general Adverse AE/SAE module for a complete list of AEs and SAEs.

End point type	Secondary
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End point timeframe:

From Treatment Day1 until Week 12

End point values	Duac	Skinoren		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108 ^[26]	109 ^[27]		
Units: Participants				
Any AE	62	76		
Any SAE	2	3		

Notes:

[26] - ITT Analysis Set

[27] - ITT Analysis Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment SAEs and non-serious AEs were collected from the start of study medication until the follow-up visit (up to 12 weeks).

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs are reported for members of the ITT Population, comprised of all participants who were randomized to treatment and received at least one dose of study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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Reporting groups

Reporting group title	Duac
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Reporting group description:

Participants topically applied a thin film of Duac gel once daily in the evening for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

Reporting group title	Skinoren
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Reporting group description:

Participants topically applied a thin film of Skinoren cream twice daily (once in the morning and once in the evening) for 12 weeks, over the entire face, avoiding the mouth and eyes. Prior to the application, participants were advised to wash their face with the soap free cleanser, rinse thoroughly with warm water, and pat the skin thoroughly dry with a soft towel. After application, the participants had to avoid washing face for 4 hours (preferably 8 hours). Oil free facial moisturizer was used, if required.

Serious adverse events	Duac	Skinoren	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 108 (1.85%)	3 / 109 (2.75%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Reproductive system and breast disorders			
Vulval haematoma			
subjects affected / exposed	1 / 108 (0.93%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Stress			
subjects affected / exposed	1 / 108 (0.93%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 108 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Brucellosis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 109 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 108 (0.00%)	1 / 109 (0.92%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Duac	Skinoren	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 108 (29.63%)	55 / 109 (50.46%)	
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 108 (14.81%)	18 / 109 (16.51%)	
occurrences (all)	26	26	
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	7 / 108 (6.48%)	22 / 109 (20.18%)	
occurrences (all)	7	24	
Application site pruritus			
subjects affected / exposed	8 / 108 (7.41%)	25 / 109 (22.94%)	
occurrences (all)	8	27	

Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	10 / 108 (9.26%) 12	20 / 109 (18.35%) 21	
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2014	4.3: Exclusion criteria 6, deletion of contraceptives; addition of exclusion criteria 9 -> to ensure consistency between exclusion criteria and section 5.7.1 permitted medications and non-drug therapies. 6.2.1.3, 6.2.2.2: Add assessment at week 0 -> to ensure consistency between time and events table and section 6.2.1.3, 6.2.2.2 6.3.8.2: Add respiratory rate -> to ensure consistency between time and events table and section 6.3.8.2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported