Clinical trial results:
A Phase IIa, 28-day treatment, multicentre, randomised, comparator-controlled, observer-blind trial with intra-individual left/right comparison to investigate the anti-psoriatic efficacy and the safety of an LAS41004 formulation in comparison to an active reference in patients with mild to moderate plaque psoriasis

Summary

EudraCT number	2013-003757-22
Trial protocol	DE
Global end of trial date	13 October 2014

Results information

Result version number	v1 (current)
This version publication date	25 June 2016
First version publication date	25 June 2016

Trial information

Trial identification

Sponsor protocol code	H553000-1309

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02180464
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Almirall Hermal GmbH
Sponsor organisation address	Scholtzstraße 3, Reinbek, Germany, 21465
Public contact	Disclosure Central Team, ALMIRALL S.A., R&D@almirall.com
Scientific contact	Disclosure Central Team, ALMIRALL S.A., R&D@almirall.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	13 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 October 2014
Global end of trial reached?	Yes
Global end of trial date	13 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the anti-psoriatic efficacy and safety of the combination of LAS41004 (bexarotene plus betamethasone dipropionate) in a topical formulation by reference to Daivobet® ointment (calcipotriol plus betamethasone dipropionate)

Protection of trial subjects:

The study was conducted in accordance with legal and regulatory requirements, as well as the general principles set forth in the International Conference on Harmonisation (ICH) Guidelines for Good Clinical Practice (GCP) and applicable local regulatory requirements and laws. As such, screening assessments were performed after the patient had agreed to participate and had signed and dated the informed consent form, and safety and tolerability were evaluated throughout the study by monitoring of adverse events, performing laboratory tests and physical examinations, and measuring vital signs

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 June 2014
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	Germany: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	36
From 65 to 84 years	4

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

30 ± 3 days prior to the first IMP administration (women) and up to 30 days prior to the first IMP administration (men), subjects underwent initial screening. Of 43 subjects screened, 3 subjects were not enrolled due to screen failure

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	Subject

Arms

Are arms mutually exclusive?	No
Arm title	LAS41004

Arm description:

Once-daily topical application of LAS41004 (bexarotene 1% plus betamethasone dipropionate 0.064%) approximately 2–6 mg/cm2 to an area of 20–300 cm2

Arm type	Experimental
Investigational medicinal product name	LAS41004
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use , Cutaneous use

Dosage and administration details:

Approximately 2 – 6 mg/cm2 of test product was applied by the patient to lesional areas (20–300 cm2) each, once daily without occlusion on 28 consecutive days. Each test product was applied once daily for a total of 28 days

Arm title	Daivobet

Arm description:

Once-daily topical application of Daivobet (calcipotriol 0.05 mg/g plus betamethasone dipropionate 0.5 mg/g [BDP 0.643 mg/g]) approximately 2–6 mg/cm2 to an area of 20–300 cm2

Arm type	Active comparator
Investigational medicinal product name	Daivobet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Cutaneous use, Topical use

Dosage and administration details:

Approximately 2–6 mg/cm2 of test product was applied by the patient to lesional areas (20–300 cm2) each, once daily without occlusion on 28 consecutive days. Each test product was applied once daily for a total of 28 days

Number of subjects in period 1	LAS41004	Daivobet
Started	40	40
Completed	40	40

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	40	40	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	46		
standard deviation	± 14.2	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	31	31	

End points

End points reporting groups

Reporting group title	LAS41004
Reporting group description:	
Once-daily topical application of LAS41004 (bexarotene 1% plus betamethasone dipropionate 0.064%) approximately 2–6 mg/cm2 to an area of 20–300 cm2	
Reporting group title	Daivobet
Reporting group description:	
Once-daily topical application of Daivobet (calcipotriol 0.05 mg/g plus betamethasone dipropionate 0.5 mg/g [BDP 0.643 mg/g]) approximately 2–6 mg/cm2 to an area of 20–300 cm2	

Primary: Change from baseline in total sign score on Day 29

End point title	Change from baseline in total sign score on Day 29
End point description:	
Total sign score (TSS) was defined as the sum of individual scores for erythema, scaling and infiltration using a 5-point scale (0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = severest possible)	
End point type	Primary
End point timeframe:	
Day 29	

End point values	LAS41004	Daivobet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: unit(s)				
arithmetic mean (standard deviation)	-4.2 (± 1.62)	-5.5 (± 1.32)		

Statistical analyses

Statistical analysis title	Day 29 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.8

Variability estimate	Standard error of the mean
Dispersion value	0.3

Secondary: Change from baseline in total sign score

End point title	Change from baseline in total sign score

End point description:

Total sign score (TSS) was defined as the sum of individual scores for erythema, scaling and infiltration using a 5-point scale (0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = severest possible)

End point type	Secondary

End point timeframe:

Up to day 29

End point values	LAS41004	Daivobet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: unit(s)				
arithmetic mean (standard deviation)				
Day 4	-1.2 (± 1.08)	-1.8 (± 1.3)		
Day 8	-2.3 (± 1.52)	-3.4 (± 1.42)		
Day 15	-3.1 (± 1.55)	-4.4 (± 1.31)		
Day 22	-3.5 (± 1.6)	-5 (± 1.29)		
Day 29	-4.2 (± 1.62)	-5.5 (± 1.32)		

Statistical analyses

Statistical analysis title	Day 4 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0066
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[1] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 8 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[2] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 15 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.9
Variability estimate	Standard error of the mean
Dispersion value	0.28

Notes:

[3] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 22 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[4] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 29 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[5] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Secondary: Change from baseline in erythema

End point title	Change from baseline in erythema

End point description:

Individual scores for erythema, scaling and infiltration were assessed using a 5-point scale (0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = severest possible)

End point type	Secondary

End point timeframe:

Up to Day 29

End point values	LAS41004	Daivobet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: unit(s)/gram				
arithmetic mean (standard deviation)				
Day 4	-0.2 (± 0.42)	-0.3 (± 0.46)		
Day 8	-0.5 (± 0.55)	-0.6 (± 0.5)		
Day 15	-0.7 (± 0.62)	-0.9 (± 0.62)		
Day 22	-0.8 (± 0.59)	-1.1 (± 0.69)		

Day 29	-1.1 (± 0.75)	-1.3 (± 0.57)		

Statistical analyses

Statistical analysis title	Day 4 LAS41004 v Daivobet
Comparison groups	Daivobet v LAS41004
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.3981
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.09

Notes:

[6] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 8 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.2461
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[7] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 15 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.0647
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[8] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 22 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.0159
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[9] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 29 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.0152
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.5

Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[10] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Secondary: Change from baseline in scaling

End point title	Change from baseline in scaling

End point description:

Individual scores for erythema, scaling and infiltration were assessed using a 5-point scale (0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = severest possible)

End point type	Secondary

End point timeframe:

Up to Day 29

End point values	LAS41004	Daivobet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: unit(s)				
arithmetic mean (standard deviation)				
Day 4	-0.6 (± 0.63)	-0.9 (± 0.61)		
Day 8	-1.1 (± 0.88)	-1.7 (± 0.89)		
Day 15	-1.4 (± 0.81)	-2 (± 0.66)		
Day 22	-1.5 (± 0.85)	-2.1 (± 0.69)		
Day 29	-1.7 (± 0.78)	-2.2 (± 0.75)		

Statistical analyses

Statistical analysis title	Day 4 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.0541
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[11] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 8 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.0003
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[12] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 15 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.0002
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[13] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 22 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	< 0
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[14] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 29 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.0015
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[15] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Secondary: Change from baseline in infiltration

End point title	Change from baseline in infiltration

End point description:

Individual scores for erythema, scaling and infiltration were assessed using a 5-point scale (0 = absent, 1 = slight, 2 = moderate, 3 = severe, 4 = severest possible)

End point type	Secondary

End point timeframe:

Up to Day 29

End point values	LAS41004	Daivobet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: unit(s)				
arithmetic mean (standard deviation)				
Day 4	-0.3 (± 0.57)	-0.7 (± 0.74)		
Day 8	-0.8 (± 0.77)	-1.1 (± 0.86)		
Day 15	-1 (± 0.73)	-1.5 (± 0.82)		
Day 22	-1.2 (± 0.77)	-1.8 (± 0.7)		

Day 29	-1.5 (± 0.85)	-2 (± 0.78)		

Statistical analyses

Statistical analysis title	Day 4 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.0021
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[16] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 8 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.0243
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.6
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[17] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 15 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	< 0
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[18] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 22 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	< 0
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[19] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 29 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	= 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.8

Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[20] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Secondary: Change from baseline in Physician's Global Assessment

End point title	Change from baseline in Physician's Global Assessment

End point description:

The overall clinical picture of psoriasis of the respective lesion was scored from severe to clear using a 6-point scale (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = moderate to severe, 5 = severe)

End point type	Secondary

End point timeframe:

Up to Day 29

End point values	LAS41004	Daivobet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: unit(s)				
arithmetic mean (standard deviation)				
Day 4	-0.4 (± 0.54)	-0.6 (± 0.6)		
Day 8	-0.7 (± 0.65)	-1 (± 0.68)		
Day 15	-1 (± 0.89)	-1.5 (± 0.68)		
Day 22	-1.1 (± 0.97)	-1.8 (± 0.8)		
Day 29	-1.5 (± 0.93)	-2 (± 0.8)		

Statistical analyses

Statistical analysis title	Day 4 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	= 0.1192
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.4
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[21] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 8 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.0133
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[22] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 15 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.0028
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.7
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[23] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 22 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[24] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Statistical analysis title	Day 29 LAS41004 v Daivobet
Comparison groups	LAS41004 v Daivobet
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	= 0.0008
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[25] - The number of participants in this analysis is automatically calculated by the database. The arms are not mutually exclusive and the number of patients in this analysis is 40, not 80

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 7 days after last study drug administration	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	LAS41004
Reporting group description:	
LAS41004 (bexarotene 1% plus betamethasone dipropionate 0.064%) once-daily topical application of approximately 2-6 mg/cm2 to an area of 20-300 cm2	
Reporting group title	Daivobet
Reporting group description:	
Once daily topical application of Daivobet (calcipotriol 0.05 mg/g plus betamethasone dipropionate 0.5 mg/g [BDP 0.643 mg/g]) approximately 2-6 mg/cm2 to an area of 20-300 cm2	

Serious adverse events	LAS41004	Daivobet	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 40 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	LAS41004	Daivobet	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 40 (10.00%)	0 / 40 (0.00%)	
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Panic attack			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 40 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 April 2014	Amendment 1 was necessary due to conditions and advice noted by the BfArM (Bundesinstitut fuer Arzneimittel und Medizinprodukte [German Federal Institute for Drugs and Medical Devices]) regarding stress and risks, inclusion and exclusion criteria, restrictions, manner of treatment, pregnancy test and measurement/assessment time points
24 April 2014	Amendment 2 was necessary due to new information regarding the analysis of stability for the LAS41004 formulation and a consequent correction of the corresponding storage conditions

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported