



Clinical trial results:

A phase II trial to evaluate the anti-psoriatic efficacy and tolerability of tazarotene in a gel formulation in patients with mild to moderate nail psoriasis - parallel group comparison

Summary

EudraCT number	2013-004519-28
Trial protocol	DE
Global end of trial date	15 May 2015

Results information

Result version number	v1 (current)
This version publication date	17 August 2016
First version publication date	17 August 2016

Trial information

Trial identification

Sponsor protocol code	H573000-1307
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	15 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 May 2015
Global end of trial reached?	Yes
Global end of trial date	15 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to assess the anti-psoriatic efficacy and tolerability of tazarotene in a gel formulation in patients with mild to moderate nail psoriasis compared to the vehicle

Protection of trial subjects:

The clinical trial was conducted in compliance with globally accepted standards of good clinical practice (as defined in the ICH E6 guideline for good clinical practice, January 1997), in agreement with the Declaration of Helsinki (Seoul, October 2008) and in keeping with German regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 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: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	64
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicentre trial conducted in 6 centres in Germany. First patient visit was in February 2014 and last patient visit was in May 2015

Pre-assignment

Screening details:

During a 4-week screening phase, 85 patients were screened and there were 19 screening failures

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LAS41006
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tazarotene
Investigational medicinal product code	LAS41006
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

LAS41006 (0.1%) or vehicle gel was topically applied with up to 40 mg gel to each of the affected fingernails (approximately 1–4 cm², each) once daily over night to each affected fingernail (at least one) during a 12-week treatment period (84 applications). Maximum daily dosage was approximately 0.4 mg tazarotene (in case all 10 fingernails affected and treated)

Immediately after each application the respective fingernail was covered with a semi-occlusive plaster overnight

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

LAS41006 (0.1%) or vehicle gel was topically applied with up to 40 mg gel to each of the affected fingernails (approximately 1–4 cm², each) once daily over night to each affected fingernail (at least one) during a 12-week treatment period (84 applications)

Immediately after each application the respective fingernail was covered with a semi-occlusive plaster overnight

Number of subjects in period 1	LAS41006	Placebo
Started	34	32
Completed	28	27
Not completed	6	5
Consent withdrawn by subject	5	4
Lost to follow-up	1	1

Baseline characteristics

Reporting groups

Reporting group title	LAS41006
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	LAS41006	Placebo	Total
Number of subjects	34	32	66
Age categorical Units: Subjects			
Adults (18-64 years)	33	31	64
From 65-84 years	1	1	2
Age continuous Units: years			
arithmetic mean	49	51.4	
standard deviation	± 13	± 10	-
Gender categorical Units: Subjects			
Female	9	14	23
Male	25	18	43

End points

End points reporting groups

Reporting group title	LAS41006
Reporting group description:	-
Reporting group title	Placebo
Reporting group description:	-

Primary: Percentage change from baseline in mNAPSI of the target fingernail

End point title	Percentage change from baseline in mNAPSI of the target fingernail
End point description:	<p>mNAPSI was a measure of severity of psoriasis affecting a target nail. The 4 quadrants of the target fingernail were assessed separately by 8 parameters - 4 reflecting nail matrix involvement (pitting, leukonychia, red spotted lunula, and plate crumbling) and 4 reflecting nail bed involvement (onycholysis, subungual hyperkeratosis, oil drops [salmon patches], and splinter haemorrhages) - using a scale of 0 (= none) to 3 (= severe)</p> <p>The mNAPSI, defined as the sum of all 8 parameters in each of the 4 quadrants of the target nail, lay between 0 and 96</p>
End point type	Primary
End point timeframe:	Day 85 (End of Treatment)

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: Percentage				
arithmetic mean (standard deviation)	-14.7 (± 39.3)	-33 (± 36.6)		

Statistical analyses

Statistical analysis title	LAS41006 v Placebo
Comparison groups	LAS41006 v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0573
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	18.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	37.3
Variability estimate	Standard error of the mean
Dispersion value	9.5

Secondary: Change from baseline in mNAPSI

End point title	Change from baseline in mNAPSI
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End point description:

mNAPSI was a measure of severity of psoriasis affecting a target nail. The 4 quadrants of the target fingernail were assessed separately by 8 parameters - 4 reflecting nail matrix involvement (pitting, leukonychia, red spotted lunula, and plate crumbling) and 4 reflecting nail bed involvement (onycholysis, subungual hyperkeratosis, oil drops [salmon patches], and splinter haemorrhages) - using a scale of 0 (= none) to 3 (= severe)

The mNAPSI, defined as the sum of all 8 parameters in each of the 4 quadrants of the target nail, lay between 0 and 96

End point type	Secondary
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End point timeframe:

Up to Day 169 (follow-up)

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[1]	32 ^[2]		
Units: Score				
arithmetic mean (standard deviation)				
Baseline	17.4 (± 5.3)	16.5 (± 3.9)		
Day 15	-0.5 (± 2.7)	-2.5 (± 3.9)		
Day 29	-1.7 (± 3.9)	-3.6 (± 5.5)		
Day 57	-3 (± 5.7)	-5.1 (± 6.9)		
Day 85 (end of treatment)	-2.6 (± 6.5)	-5.4 (± 6.5)		
Day 169 (follow-up)	-3.6 (± 5.5)	-5.3 (± 6.8)		

Notes:

[1] - At Day 169, N=28

[2] - At Day 169, N=27

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of mNAPSI-50 and -75 responders

End point title	Percentage of mNAPSI-50 and -75 responders
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End point description:

mNAPSI was a measure of severity of psoriasis affecting a target nail. The 4 quadrants of the target fingernail were assessed separately by 8 parameters - 4 reflecting nail matrix involvement (pitting, leukonychia, red spotted lunula, and plate crumbling) and 4 reflecting nail bed involvement (onycholysis, subungual hyperkeratosis, oil drops [salmon patches], and splinter haemorrhages) - using

a scale of 0 (= none) to 3 (= severe)

The mNAPSI, defined as the sum of all 8 parameters in each of the 4 quadrants of the target nail, lay between 0 and 96

mNAPSI-50, mNAPSI-75 and mNAPSI-90 defined as proportion of patients achieving an improvement of $\geq 50\%$, $\geq 75\%$ and $\geq 90\%$, respectively, in % change in mNAPSI

End point type	Secondary
End point timeframe:	
Up to Day 169 (follow-up)	

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[3]	32 ^[4]		
Units: Percentage				
mNAPSI-50 Day 15	0	13		
mNAPSI-50 Day 29	9	22		
mNAPSI-50 Day 57	16	28		
mNAPSI-50 Day 85 (end of treatment)	25	34		
mNAPSI-50 Day 169 (follow-up)	18	37		
mNAPSI-75 Day 15	0	0		
mNAPSI-75 Day 29	0	6		
mNAPSI-75 Day 57	6	16		
mNAPSI-75 Day 85 (end of treatment)	6	16		
mNAPSI-75 Day 169 (follow-up)	4	15		

Notes:

[3] - On Day 169, N=28

[4] - On Day 169, N=27

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of mNAPSI-90 responders

End point title	Percentage of mNAPSI-90 responders
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End point description:

mNAPSI was a measure of severity of psoriasis affecting a target nail. The 4 quadrants of the target fingernail were assessed separately by 8 parameters - 4 reflecting nail matrix involvement (pitting, leukonychia, red spotted lunula, and plate crumbling) and 4 reflecting nail bed involvement (onycholysis, subungual hyperkeratosis, oil drops [salmon patches], and splinter hemorrhages) - using a scale of 0 (= none) to 3 (= severe)

The mNAPSI, defined as the sum of all 8 parameters in each of the 4 quadrants of the target nail, lay between 0 and 96

mNAPSI-50, mNAPSI-75 and mNAPSI-90 defined as proportion of patients achieving an improvement of $\geq 50\%$, $\geq 75\%$ and $\geq 90\%$, respectively, in % change in mNAPSI

End point type	Secondary
End point timeframe:	
Up to Day 169 (follow-up)	

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[5]	32 ^[6]		
Units: Percentage				
mNAPSI-90 Day 15	0	0		
mNAPSI-90 Day 29	0	0		
mNAPSI-90 Day 57	0	3		
mNAPSI-90 Day 85 (end of treatment)	0	9		
mNAPSI-90 Day 169 (follow-up)	0	7		

Notes:

[5] - On Day 169, N=28

[6] - On Day 169, N=28

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mNAPSI nail bed total scores

End point title	Change from baseline in mNAPSI nail bed total scores
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End point description:

End point type	Secondary
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End point timeframe:

Up to Day 169 (follow-up)

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[7]	32 ^[8]		
Units: Score				
arithmetic mean (standard deviation)				
Baseline	8.8 (± 3.5)	9.2 (± 3.4)		
Day 15	-0.3 (± 1.9)	-1.7 (± 2.8)		
Day 29	-1.3 (± 2.8)	-1.9 (± 3.9)		
Day 57	-1.4 (± 3.8)	-2.9 (± 4.5)		
Day 85 (end of treatment)	-1.4 (± 4.9)	-2.1 (± 5)		
Day 169 (follow-up)	-1.8 (± 3.7)	-2.2 (± 5.1)		

Notes:

[7] - At Day 169, N=28

[8] - At Day 169, N=27

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mNAPSI nail matrix bed total scores

End point title	Change from baseline in mNAPSI nail matrix bed total scores
End point description:	
End point type	Secondary
End point timeframe:	
Up to Day 169 (follow-up)	

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[9]	32 ^[10]		
Units: Score				
arithmetic mean (standard deviation)				
Baseline	8.6 (± 6.1)	7.3 (± 4.9)		
Day 15	-0.2 (± 1.7)	-0.8 (± 1.9)		
Day 29	-0.4 (± 2.6)	-1.7 (± 3)		
Day 57	-1.6 (± 3.6)	-2.2 (± 2.9)		
Day 85 (end of treatment)	-1.2 (± 3.3)	-2.7 (± 3.4)		
Day 169 (follow-up)	-1.8 (± 3.7)	-3.1 (± 4.2)		

Notes:

[9] - At Day 169, N=28

[10] - At Day 169, N=27

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in NAPSI of all 10 fingernails (including target fingernail)

End point title	Change from baseline in NAPSI of all 10 fingernails (including target fingernail)
End point description:	
The NAPSI assessed the presence of nail matrix (pitting, leukonychia, red spotted lunula, or plate crumbling) and nail bed (onycholysis, subungual hyperkeratosis, oil drops [salmon patches], or splinter hemorrhages) involvement in each quadrant of all 10 fingernails	
The NAPSI total score was defined as the total number of involved quadrants of all 10 fingernails of the nail matrix and nail bed assessments, ranging from 0 to 80	
End point type	Secondary
End point timeframe:	
Up to Day 169 (follow-up)	

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[11]	32 ^[12]		
Units: Score				
arithmetic mean (standard deviation)				
Baseline	35.7 (± 14)	34.6 (± 14.6)		

Day 15	-0.1 (± 2.6)	-1.9 (± 5.6)		
Day 29	-0.8 (± 4.7)	-2.3 (± 9.7)		
Day 57	-1.3 (± 5.8)	-3.4 (± 11.3)		
Day 85 (end of treatment)	-0.3 (± 6.2)	-3.4 (± 12.8)		
Day 169 (follow-up)	-1 (± 7.7)	-3.3 (± 11.4)		

Notes:

[11] - On Day 169, N=28

[12] - On Day 169, N=27

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in NAPPA-QOL global score

End point title	Change from baseline in NAPPA-QOL global score
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End point description:

NAPPA-QOL was a 20-item nail-specific quality of life questionnaire which assesses specific quality of life conditions in the past week

Answers were given in Likert scales from 0 to 4: 0 = 'not at all'; 1 = 'somewhat'; 2 = 'moderately'; 3 = 'quite'; 4 = 'very'

The NAPPA-QOL global score was determined as average of the 20 items

End point type	Secondary
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End point timeframe:

Up to Day 169 (follow-up)

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31 ^[13]	31 ^[14]		
Units: Score				
arithmetic mean (standard deviation)				
Baseline	1.53 (± 0.62)	1.56 (± 0.8)		
Day 15	-0.35 (± 0.43)	-0.31 (± 0.43)		
Day 29	-0.42 (± 0.48)	-0.38 (± 0.46)		
Day 57	-0.47 (± 0.58)	-0.39 (± 0.48)		
Day 85 (end of treatment)	-0.46 (± 0.62)	-0.43 (± 0.63)		
Day 169 (follow-up)	-0.4 (± 0.52)	-0.36 (± 0.63)		

Notes:

[13] - On Day 169, N=28

[14] - On Day 169, N=27

Statistical analyses

No statistical analyses for this end point

Secondary: NAPPA-PBI global score

End point title	NAPPA-PBI global score
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End point description:

The NAPPA-PBI global score, an importance-weighted sum of 24 benefit scores

The weights were derived from patient defined needs as assessed in a 24-item questionnaire at baseline

End point type	Secondary
End point timeframe:	
Day 85 (end of treatment) and Day 169 (follow-up)	

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31 ^[15]	28 ^[16]		
Units: Score				
arithmetic mean (standard deviation)				
Day 85 (end of treatment)	0.56 (± 0.85)	0.71 (± 0.91)		
Day 169 (follow-up)	0.72 (± 0.88)	0.83 (± 0.93)		

Notes:

[15] - On Day 169, N=28

[16] - On Day 169, N=25

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in NAPPA-CLIN

End point title	Change from baseline in NAPPA-CLIN
End point description:	
NAPPA-CLIN has been developed from the NAPSI score, which in its original version comprises the assessment of matrix and nail bed involvement in every finger and toe by 8 criteria for each nail	
The NAPPA-CLIN is a simplified version of the NAPSI. In this trial it only assessed the least and the worst involved fingernail of both hands. Thus, the NAPPA-CLIN score for hands, as the sum of the least and the worst involvement, ranged from 0 to 16 empirically	
End point type	Secondary
End point timeframe:	
Up to Day 169 (follow-up)	

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: Score				
arithmetic mean (standard deviation)				
Baseline	8.1 (± 2.2)	7.8 (± 2.3)		
Day 15	0.1 (± 1.5)	-0.1 (± 1.4)		
Day 29	-0.2 (± 1.9)	-0.6 (± 2.2)		
Day 57	-0.3 (± 2)	-0.7 (± 2.4)		
Day 85 (end of treatment)	0 (± 1.4)	-0.5 (± 2.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Physician's global assessment score

End point title Physician's global assessment score

End point description:

End point type Secondary

End point timeframe:

Day 85 (end of treatment)

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31		
Units: Percentage				
0 = cure	0	0		
1 = almost clear	0	16		
2 = visible signs	19	29		
3 = distinctly visible, marked signs	81	55		

Statistical analyses

No statistical analyses for this end point

Secondary: Patient's global assessment score

End point title Patient's global assessment score

End point description:

Patient's global assessment of efficacy performed as average over all treated fingernails

End point type Secondary

End point timeframe:

Day 85 (end of treatment)

End point values	LAS41006	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	31		
Units: Percentage				
0 = very good	0	3		
1 = good	13	16		
2 = acceptable	16	16		
3 = poor	71	65		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 169 (follow-up) ± 7 days

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	LAS41006
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	LAS41006	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 32 (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: 5 %

Non-serious adverse events	LAS41006	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 34 (2.94%)	2 / 32 (6.25%)	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 34 (2.94%)	2 / 32 (6.25%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 August 2014	Inclusion of two further trial centres in the trial conduct to recruit more patients and changes of protocol sections necessary for clarification and better readability

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported