



## 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 |
|-----------------------|--------------|

#### 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      |
| <b>Arm title</b>             | 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 cm<sup>2</sup>, 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

|                                        |             |
|----------------------------------------|-------------|
| <b>Arm title</b>                       | 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 cm<sup>2</sup>, 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

| <b>Number of subjects in period 1</b> | 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<br>Units: Subjects    |          |         |       |
| Adults (18-64 years)                  | 33       | 31      | 64    |
| From 65-84 years                      | 1        | 1       | 2     |
| Age continuous<br>Units: years        |          |         |       |
| arithmetic mean                       | 49       | 51.4    |       |
| standard deviation                    | ± 13     | ± 10    | -     |
| Gender categorical<br>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:

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            | 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 ( $\pm$ 39.3) | -33 ( $\pm$ 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 |
|-----------------|--------------------------------|

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 |
|----------------|-----------|

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 <sup>[1]</sup> | 32 <sup>[2]</sup> |  |  |
| 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 |
|-----------------|--------------------------------------------|

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 <sup>[3]</sup> | 32 <sup>[4]</sup> |  |  |
| 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 |
|-----------------|------------------------------------|

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 <sup>[5]</sup> | 32 <sup>[6]</sup> |  |  |
| 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 |
|-----------------|------------------------------------------------------|

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 <sup>[7]</sup> | 32 <sup>[8]</sup> |  |  |
| 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 <sup>[9]</sup> | 32 <sup>[10]</sup> |  |  |
| 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 <sup>[11]</sup> | 32 <sup>[12]</sup> |  |  |
| 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 |
|-----------------|------------------------------------------------|

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 |
|----------------|-----------|

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 <sup>[13]</sup> | 31 <sup>[14]</sup> |  |  |
| 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 |
|-----------------|------------------------|

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 <sup>[15]</sup> | 28 <sup>[16]</sup> |  |  |
| 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)  $\pm 7$  days

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | LAS41006 |
|-----------------------|----------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

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