



## Clinical trial results:

**A multicenter, randomized, parallel, double-blind, clinical trial study to assess the efficacy and safety of Fluocinolone Acetonide 0.025% Otic Solution compared to Placebo in patients with otic eczema.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2011-004172-11 |
| Trial protocol           | ES             |
| Global end of trial date | 22 March 2013  |

### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 16 February 2016   |
| First version publication date    | 09 July 2015   |
| Summary attachment (see zip file) | FLUOTIII/11ES01 Synopsis CSR (FLUOTIII_11ES01 Synopsis CSR Final 25June2013.pdf) |

### Trial information

#### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | FLUOTIII/11ES01 |
|-----------------------|-----------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01996748 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Laboratorios SALVAT, S.A.  |
| Sponsor organisation address | Gall, 30-36, Esplugues de Llobregat, Spain, 08950  |
| Public contact               | Medical Department, Laboratorios SALVAT, S.A., +34 933946469, clinicaltrials@salvatbiotech.com |
| Scientific contact           | Medical Department, Laboratorios SALVAT, S.A., +34 933946470, ejimenezv@salvatbiotech.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:

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**Results analysis stage**

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|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 22 March 2013 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 22 March 2013 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 22 March 2013 |
| Was the trial ended prematurely?                     | No            |

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the efficacy of Fluocinolone Acetonide 0.025% otic solution compared to placebo for the reduction of itching after 8 days of starting treatment in patients with otic eczema.

Protection of trial subjects:

Not applicable

Background therapy:

Not applicable

Evidence for comparator:

The availability of medical treatment is very diverse depending on the EU country; there is not a "gold standard" for this condition. In the absence of a general well established treatment and based on the NOTE FOR GUIDANCE ON CHOICE OF CONTROL GROUP IN CLINICAL TRIALS (CPMP/ICH/364/96), a placebo controlled trial was considered the best design option.

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 09 March 2012 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |            |
|--------------------------------------|------------|
| Country: Number of subjects enrolled | Spain: 135 |
| Worldwide total number of subjects   | 135        |
| EEA total number of subjects         | 135        |

Notes:

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**Subjects enrolled per age group**

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|   |     |
|---|-----|
| 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)                      | 109 |
| From 65 to 84 years                       | 26  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

The recruitment period was from 9th March 2012 to 22nd March 2013.

### Pre-assignment

Screening details:

Male and female patients aged 12 years or older with clinical diagnosis of otic eczema suitable for local treatment according to the investigator.

Patients must have moderate or severe itching in the ear canal (with or without involvement of the pinna), and otoscopic image of scaling in the ear canal skin.

### Period 1

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

Blinding implementation details:

Both Fluocinolone Acetonide 0.025% otic solution and the placebo had identical organoleptical characteristics. The randomization data remained strictly confidential and only authorized persons had access, until the definitive creation of the database.

In case of emergency, for opening the randomization codes, there were a complete set of emergency codes at the investigator's site. The opening of said codes had to be reported to the study monitor immediately and duly recorded.

### Arms

|  |  |
|--|--|
| Are arms mutually exclusive?           | Yes  |
| <b>Arm title</b>                       | Fluocinolone acetonide                       |
| Arm description: -                     |  |
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Fluocinolone acetonide                       |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Ear drops, solution in single-dose container |
| Routes of administration               | Auricular use                                |

Dosage and administration details:

Administer the contents of one 0.40 ml single dose vial twice a day to the affected ear(s) for seven days

|  |  |
|--|--|
| <b>Arm title</b>                       | Placebo                                      |
| Arm description: -                     |  |
| Arm type                               | Placebo                                      |
| Investigational medicinal product name | Placebo                                      |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Ear drops, solution in single-dose container |
| Routes of administration               | Auricular use                                |

Dosage and administration details:

Administer the contents of one 0.40ml single-dose vial twice a day to the affected ear(s) for seven days

| <b>Number of subjects in period 1</b> | Fluocinolone<br>acetoneide | Placebo |
|---------------------------------------|----------------------------|---------|
| Started                               | 66                         | 69      |
| Completed                             | 58                         | 63      |
| Not completed                         | 8                          | 6       |
| Physician decision                    | 2                          | -       |
| Consent withdrawn by subject          | -                          | 1       |
| Adverse event, non-fatal              | 1                          | 4       |
| peronal reasons                       | 1                          | -       |
| Lost to follow-up                     | 4                          | 1       |

## Baseline characteristics

## End points

### End points reporting groups

|                                |                        |
|--------------------------------|------------------------|
| Reporting group title          | Fluocinolone acetonide |
| Reporting group description: - |                        |
| Reporting group title          | Placebo                |
| Reporting group description: - |                        |

### Primary: Change in itching on Days 4-8 compared to baseline

|                        |  |
|------------------------|--|
| End point title        | Change in itching on Days 4-8 compared to baseline |
| End point description: |  |
| End point type         | Primary  |
| End point timeframe:   |  |
| Day 4-8                |  |

| End point values                               | Fluocinolone acetonide | Placebo                |  |  |
|--|------------------------|------------------------|--|--|
| Subject group type                             | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed                    | 63                     | 68                     |  |  |
| Units: scores                                  |                        |                        |  |  |
| arithmetic mean (inter-quartile range (Q1-Q3)) | -1.63 (-2 to -1.1)     | -1.25 (-1.75 to -0.84) |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | ANCOVA on the itching change from baseline |
| Comparison groups                       | Fluocinolone acetonide v Placebo           |
| Number of subjects included in analysis | 131  |
| Analysis specification                  | Pre-specified                              |
| Analysis type                           | superiority                                |
| P-value                                 | < 0.05                                     |
| Method                                  | ANCOVA                                     |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All study period

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Fluocinolone Acetonide |
|-----------------------|------------------------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events                            | Fluocinolone Acetonide | Placebo        |  |
|---|------------------------|----------------|--|
| Total subjects affected by serious adverse events |                        |                |  |
| subjects affected / exposed                       | 0 / 66 (0.00%)         | 0 / 69 (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                            | Fluocinolone Acetonide | Placebo         |  |
|---|------------------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                        |                 |  |
| subjects affected / exposed                           | 5 / 66 (7.58%)         | 9 / 69 (13.04%) |  |
| General disorders and administration site conditions  |                        |                 |  |
| Application site pruritus                             |                        |                 |  |
| subjects affected / exposed                           | 1 / 66 (1.52%)         | 0 / 69 (0.00%)  |  |
| occurrences (all)                                     | 1                      | 0               |  |
| Ear and labyrinth disorders                           |                        |                 |  |
| Ear discomfort  |                        |                 |  |
| subjects affected / exposed                           | 3 / 66 (4.55%)         | 4 / 69 (5.80%)  |  |
| occurrences (all)                                     | 4                      | 4               |  |
| Ear disorder  |                        |                 |  |
| subjects affected / exposed                           | 1 / 66 (1.52%)         | 0 / 69 (0.00%)  |  |
| occurrences (all)                                     | 1                      | 0               |  |



|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Ear pain                    |                |                |  |
| subjects affected / exposed | 0 / 66 (0.00%) | 1 / 69 (1.45%) |  |
| occurrences (all)           | 0              | 1              |  |
| Otitis externa              |                |                |  |
| subjects affected / exposed | 0 / 66 (0.00%) | 4 / 69 (5.80%) |  |
| occurrences (all)           | 0              | 4              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment                  |
|--------------|----------------------------|
| 29 June 2012 | Inclusion of a new centre. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported