



## Clinical trial results: Safety and Efficacy Evaluation of Topical Moxidex Otic Solution in the Treatment of Acute Otitis Externa (AOE)

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-000641-39 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 25 July 2007   |

### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 08 August 2018 |
| First version publication date | 08 August 2018 |

### Trial information

#### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | C-05-37 |
|-----------------------|---------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Alcon Research Ltd  |
| Sponsor organisation address | 6201 S. Freeway, Fort Worth, TX, United States, 76134   |
| Public contact               | Ophthalmology Unit, Novartis Pharmaceuticals , + 44<br>0127666733385, linda.masson@novartis.com |
| Scientific contact           | Ophthalmology Unit, Novartis Pharmaceuticals , + 44<br>0127666733385, linda.masson@novartis.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? | Yes |

Notes:

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**Results analysis stage**

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 25 July 2007 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 25 July 2007 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 25 July 2007 |
| Was the trial ended prematurely?                     | No           |

Notes:

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**General information about the trial**

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of topical Moxidex solution for the treatment of acute otitis externa (AOE).

Protection of trial subjects:

Prior to the start of the study, the study protocol, the informed consent and assent documents, patient instruction sheets, the Investigator's Brochure, as well as any advertising materials used to recruit patients were submitted to institutional review boards (IRBs) and independent ethics committees (IECs). The IRB/IECs reviewed all documents and approved required documents; copies of the approval letters were provided to Alcon. Consistent with both the IRB/IEC's requirements and all applicable regulations, the Investigators periodically provided study updates to the IRB/IEC. A patient or parent/legal guardian (if necessary, a legally authorized representative) provided informed consent, and children signed an approved assent form when appropriate. This study was conducted in accordance with Good Clinical Practices (GCP) and the ethical principles that have their origins in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 26 June 2006 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

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**Population of trial subjects****Subjects enrolled per country**

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 268 |
| Worldwide total number of subjects   | 268                |
| EEA total number of subjects         | 0                  |

Notes:

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**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)                 | 74 |

|                      |     |
|----------------------|-----|
| Adults (18-64 years) | 181 |
| From 65 to 84 years  | 12  |
| 85 years and over    | 1   |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited from 40 study centers located in the United States.

### Pre-assignment

Screening details:

This reporting group includes all subjects who received drug (Intent-to-Treat (ITT) Analysis Set).

### Period 1

|                              |                          |
|------------------------------|--------------------------|
| Period 1 title               | Overall (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>             | Moxidex solution |

Arm description:

Moxifloxacin 0.5%/dexamethasone phosphate 0.1% solution, 4 drops twice daily (morning and evening), for 7 days

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | moxifloxacin 0.5%/dexamethasone phosphate 0.1% solution |
| Investigational medicinal product code |   |
| Other name                             | Moxidex   |
| Pharmaceutical forms                   | Ear drops, solution                                     |
| Routes of administration               | Auricular use   |

Dosage and administration details:

4 drops BID for 7 days

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | Moxifloxacin Solution |
|------------------|-----------------------|

Arm description:

Moxifloxacin hydrochloride 0.5% solution, 4 drops twice daily (morning and evening), for 7 days

|  |  |
|--|--|
| Arm type                               | Active comparator                        |
| Investigational medicinal product name | Moxifloxacin hydrochloride 0.5% solution |
| Investigational medicinal product code |  |
| Other name                             | Moxifloxacin                             |
| Pharmaceutical forms                   | Ear drops, solution                      |
| Routes of administration               | Auricular use                            |

Dosage and administration details:

4 drops BID for 7 days

| <b>Number of subjects in period 1</b> | Moxidex solution | Moxifloxacin Solution |
|---------------------------------------|------------------|-----------------------|
| Started                               | 131              | 137                   |
| Completed                             | 115              | 121                   |
| Not completed                         | 16               | 16                    |
| Treatment failure                     | 5                | 7                     |
| Adverse event, non-fatal              | 6                | 5                     |
| Inclusion/exclusion violation         | 2                | -                     |
| Other                                 | 1                | -                     |
| Decision unrelated to an AE           | 1                | 2                     |
| Lost to follow-up                     | -                | 2                     |
| Noncompliance                         | 1                | -                     |

## Baseline characteristics

### Reporting groups

|  |                       |
|--|-----------------------|
| Reporting group title  | Moxidex solution      |
| Reporting group description:<br>Moxifloxacin 0.5%/dexamethasone phosphate 0.1% solution, 4 drops twice daily (morning and evening), for 7 days |                       |
| Reporting group title  | Moxifloxacin Solution |
| Reporting group description:<br>Moxifloxacin hydrochloride 0.5% solution, 4 drops twice daily (morning and evening), for 7 days                |                       |

| Reporting group values    | Moxidex solution | Moxifloxacin Solution | Total |
|---------------------------|------------------|-----------------------|-------|
| Number of subjects        | 131              | 137                   | 268   |
| Age categorical           |                  |                       |       |
| ITT Analysis Set.         |                  |                       |       |
| Units: Subjects           |                  |                       |       |
| Adolescents (12-17 years) | 35               | 39                    | 74    |
| Adults (18-64 years)      | 88               | 93                    | 181   |
| From 65-84 years          | 8                | 4                     | 12    |
| 85 years and over         | 0                | 1                     | 1     |
| Gender categorical        |                  |                       |       |
| Units: Subjects           |                  |                       |       |
| Female                    | 66               | 73                    | 139   |
| Male                      | 65               | 64                    | 129   |

## End points

### End points reporting groups

|  |                       |
|--|-----------------------|
| Reporting group title  | Moxidex solution      |
| Reporting group description:<br>Moxifloxacin 0.5%/dexamethasone phosphate 0.1% solution, 4 drops twice daily (morning and evening), for 7 days |                       |
| Reporting group title  | Moxifloxacin Solution |
| Reporting group description:<br>Moxifloxacin hydrochloride 0.5% solution, 4 drops twice daily (morning and evening), for 7 days                |                       |

### Primary: Time to complete relief of ear pain

|  |                                     |
|--|-------------------------------------|
| End point title  | Time to complete relief of ear pain |
| End point description:<br>Complete relief of ear pain was defined as occurring on the first day that ear pain was completely relieved and remained completely relieved for all subsequent diary entries. Subject reported ear pain relief was assessed twice daily using an interactive voice recognition phone-in diary system (IVRS) and graded on a scale of 0 (complete relief of ear pain) to 6 (very much worsening of ear pain). This analysis set included all subjects who received drug, met pre-randomization inclusion and exclusion criteria and were pathogen positive for bacteria on Day 1 (Modified ITT (MITT) Analysis Set). |                                     |
| End point type   | Primary                             |
| End point timeframe:<br>Up to Day 11 (Test of Cure (TOC))  |                                     |

| End point values                 | Moxidex solution   | Moxifloxacin Solution |  |  |
|----------------------------------|--------------------|-----------------------|--|--|
| Subject group type               | Reporting group    | Reporting group       |  |  |
| Number of subjects analysed      | 127                | 129                   |  |  |
| Units: units on a scale          |                    |                       |  |  |
| median (confidence interval 95%) | 7.0 (6.50 to 8.00) | 7.0 (6.00 to 9.00)    |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Time to complete relief of ear pain      |
| Comparison groups                       | Moxifloxacin Solution v Moxidex solution |
| Number of subjects included in analysis | 256                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.5511                                 |
| Method                                  | Logrank                                  |

### Secondary: Percentage of subjects with clinical cure

|  |   |
|--|---|
| End point title  | Percentage of subjects with clinical cure |
| End point description:<br>A clinical response of resolved/cured as evaluated by the Investigator at Visit 4 was considered a clinical cure. MITT Analysis Set. |   |
| End point type   | Secondary                                 |
| End point timeframe:<br>Day 11 (TOC)   |   |

| End point values              | Moxidex solution | Moxifloxacin Solution |  |  |
|-------------------------------|------------------|-----------------------|--|--|
| Subject group type            | Reporting group  | Reporting group       |  |  |
| Number of subjects analysed   | 127              | 129                   |  |  |
| Units: percentage of subjects |                  |                       |  |  |
| number (not applicable)       | 85.0             | 82.2                  |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Clinical Cure                            |
| Comparison groups                       | Moxidex solution v Moxifloxacin Solution |
| Number of subjects included in analysis | 256                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.5354                                 |
| Method                                  | Chi-squared                              |

### Secondary: Percentage of subjects for microbiological outcome

|  |  |
|--|--|
| End point title  | Percentage of subjects for microbiological outcome |
| End point description:<br>The eradication of pre-therapy pathogens was assessed at the TOC visit. Bacterial response (success or failure) was calculated. MITT Analysis Set. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Day 11 (TOC)   |  |

| End point values              | Moxidex solution | Moxifloxacin Solution |  |  |
|-------------------------------|------------------|-----------------------|--|--|
| Subject group type            | Reporting group  | Reporting group       |  |  |
| Number of subjects analysed   | 127              | 129                   |  |  |
| Units: percentage of subjects |                  |                       |  |  |
| number (not applicable)       |                  |                       |  |  |
| Success                       | 85.0             | 82.2                  |  |  |
| Failure                       | 15.0             | 17.8                  |  |  |



## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Microbiological outcome - Treatment Failure |
| Comparison groups                       | Moxidex solution v Moxifloxacin Solution    |
| Number of subjects included in analysis | 256   |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           | superiority                                 |
| P-value                                 | = 0.5354                                    |
| Method                                  | Chi-squared                                 |

## Secondary: Percentage of subjects with treatment failure

|   |   |
|---|---|
| End point title   | Percentage of subjects with treatment failure |
| End point description:<br>Subjects who had no clinically relevant response to the medication or whose symptoms worsened after at least 2 full days of treatment with the study medication could be considered "treatment failures."<br>MITT Analysis Set. |   |
| End point type  | Secondary                                     |
| End point timeframe:<br>Day 11 (TOC)  |   |

|                               |                  |                       |  |  |
|-------------------------------|------------------|-----------------------|--|--|
| <b>End point values</b>       | Moxidex solution | Moxifloxacin Solution |  |  |
| Subject group type            | Reporting group  | Reporting group       |  |  |
| Number of subjects analysed   | 127              | 129                   |  |  |
| Units: percentage of subjects |                  |                       |  |  |
| number (not applicable)       | 15.0             | 17.8                  |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Treatment failure                        |
| Comparison groups                       | Moxidex solution v Moxifloxacin Solution |
| Number of subjects included in analysis | 256                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.5354                                 |
| Method                                  | Chi-squared                              |



## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Adverse events (AEs) are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

This analysis population includes all subjects who received study drug (Safety Analysis Set). Only total subjects affected by non-serious AEs that occurred at >5% are reported.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Moxidex solution |
|-----------------------|------------------|

Reporting group description:

Moxifloxacin 0.5%/dexamethasone phosphate 0.1% solution, 4 drops twice daily (morning and evening), for 7 days

|                       |                       |
|-----------------------|-----------------------|
| Reporting group title | Moxifloxacin Solution |
|-----------------------|-----------------------|

Reporting group description:

Moxifloxacin hydrochloride 0.5% solution, 4 drops twice daily (morning and evening), for 7 days

| Serious adverse events                            | Moxidex solution | Moxifloxacin Solution |  |
|---|------------------|-----------------------|--|
| Total subjects affected by serious adverse events |                  |                       |  |
| subjects affected / exposed                       | 0 / 131 (0.00%)  | 0 / 137 (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                            | Moxidex solution | Moxifloxacin Solution |  |
|---|------------------|-----------------------|--|
| Total subjects affected by non-serious adverse events |                  |                       |  |
| subjects affected / exposed                           | 0 / 131 (0.00%)  | 0 / 137 (0.00%)       |  |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events occurred above the 5% threshold.

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported