



## Clinical trial results:

### Safety and Efficacy Evaluation of Topical Moxidex Otic Solution Compared to Moxifloxacin Solution in the Treatment of Acute Otitis Media with Otorrhea through Tympanostomy Tubes (AOMT)

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2018-000640-26   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 04 February 2009 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 23 August 2018 |
| First version publication date | 23 August 2018 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | C-05-36 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00579189 |
| 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 0127666733385, linda.masson@novartis.com |
| Scientific contact           | Ophthalmology Unit, Novartis Pharmaceuticals , + 44 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:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 04 February 2009 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 04 February 2009 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 04 February 2009 |
| Was the trial ended prematurely?                     | No               |

Notes:

## 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 otic solution for the treatment of subjects with acute otitis media with tympanostomy tubes (AOMT) and to compare Moxidex otic solution with Moxifloxacin solution for cessation of otorrhea.

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                          | 22 February 2006 |
| 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 | United States: 776 |
| Worldwide total number of subjects   | 776                |
| EEA total number of subjects         | 0                  |

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)  | 377 |
| Children (2-11 years)                     | 395 |
| Adolescents (12-17 years)                 | 4   |

|                      |   |
|----------------------|---|
| Adults (18-64 years) | 0 |
| From 65 to 84 years  | 0 |
| 85 years and over    | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited at 48 sites located in the United States.

### Pre-assignment

Screening details:

This reporting group includes all randomized and treated subjects (776).

### 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 hydrochloride 0.5%/Dexamethasone phosphate 0.1%, 4 drops into the infected ear(s), 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 twice daily (BID) for 7 days

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

Arm description:

Moxifloxacin hydrochloride 0.5%, 4 drops into the infected ear(s), 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                                       | 389              | 387                   |
| Completed                                     | 302              | 264                   |
| Not completed                                 | 87               | 123                   |
| Treatment failure                             | 30               | 50                    |
| Baseline culture results positive for Strep A | 7                | 8                     |
| Adverse event, non-fatal                      | 35               | 40                    |
| Inclusion/exclusion violation                 | 3                | 4                     |
| Baseline culture results positive for yeast   | 1                | 4                     |
| Decision unrelated to an AE                   | 1                | 3                     |
| Lost to follow-up                             | 3                | 1                     |
| Noncompliance                                 | 1                | 4                     |
| Other - Reason not given                      | 6                | 9                     |

## Baseline characteristics

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Moxidex Solution |
|-----------------------|------------------|

Reporting group description:

Moxifloxacin hydrochloride 0.5%/Dexamethasone phosphate 0.1%, 4 drops into the infected ear(s), twice daily (morning and evening), for 7 days

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

Reporting group description:

Moxifloxacin hydrochloride 0.5%, 4 drops into the infected ear(s), twice daily (morning and evening), for 7 days

| Reporting group values  | Moxidex Solution | Moxifloxacin Solution | Total |
|---|------------------|-----------------------|-------|
| Number of subjects  | 389              | 387                   | 776   |
| Age categorical   |                  |                       |       |
| This analysis population includes all subjects who received drug. Subjects were analysed based on planned treatment group (Intent-to-Treat (ITT) Analysis Set). |                  |                       |       |
| Units: Subjects   |                  |                       |       |
| Infants and toddlers (28 days-23 months)  | 201              | 176                   | 377   |
| Children (2-11 years)   | 184              | 211                   | 395   |
| Adolescents (12-17 years)   | 4                | 0                     | 4     |
| Gender categorical  |                  |                       |       |
| ITT Analysis Set  |                  |                       |       |
| Units: Subjects   |                  |                       |       |
| Female  | 166              | 159                   | 325   |
| Male  | 223              | 228                   | 451   |

## End points

### End points reporting groups

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

### Primary: Time to Cessation of Otorrhea

|  |                               |
|--|-------------------------------|
| End point title  | Time to Cessation of Otorrhea |
| End point description:<br>Time to cessation of otorrhea was defined as the time (in days) to the cessation of otorrhea (i.e. absence of otorrhea), calculated as the number of days from surgery to the absence of otorrhea in both ears, as recorded by the parent/guardian via the patient diary. This analysis set includes 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 15 (Test of Cure (TOC))  |                               |

| End point values                 | Moxidex Solution | Moxifloxacin Solution |  |  |
|----------------------------------|------------------|-----------------------|--|--|
| Subject group type               | Reporting group  | Reporting group       |  |  |
| Number of subjects analysed      | 298              | 305                   |  |  |
| Units: days                      |                  |                       |  |  |
| median (confidence interval 95%) | 3.0 (2.5 to 3.5) | 5.0 (4.0 to 5.5)      |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Time to cessation of otorrhea            |
| Comparison groups                       | Moxidex Solution v Moxifloxacin Solution |
| Number of subjects included in analysis | 603                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.001                                  |
| Method                                  | Logrank                                  |

### Secondary: Percentage of subjects with clinical cure at TOC

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects with clinical cure at TOC |
|-----------------|--|

End point description:

Clinical Cure was defined as a clinical response of resolved/cured (i.e. otorrhea absent) or improved/ not changed/ worsened (i.e. otorrhea present) as evaluated by the Investigator. Reported as a percentage. MITT Analysis Set.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 15 (TOC)         |           |

| End point values              | Moxidex Solution | Moxifloxacin Solution |  |  |
|-------------------------------|------------------|-----------------------|--|--|
| Subject group type            | Reporting group  | Reporting group       |  |  |
| Number of subjects analysed   | 298              | 305                   |  |  |
| Units: percentage of subjects |                  |                       |  |  |
| number (not applicable)       |                  |                       |  |  |
| Absent                        | 84.6             | 71.5                  |  |  |
| Present                       | 15.4             | 28.5                  |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Clinical cure at TOC                     |
| Comparison groups                       | Moxidex Solution v Moxifloxacin Solution |
| Number of subjects included in analysis | 603                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.0001                                 |
| Method                                  | Chi-squared                              |

### Secondary: Percentage of subjects for microbiological outcome at TOC

|   |   |
|---|---|
| End point title   | Percentage of subjects for microbiological outcome at TOC |
| End point description:  |   |
| Microbiological outcome (success or failure of eradication of pre-therapy pathogens ) was measured by bacterial response at the TOC visit. MITT Analysis Set. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Day 15 (TOC)  |   |



| <b>End point values</b>       | Moxidex Solution | Moxifloxacin Solution |  |  |
|-------------------------------|------------------|-----------------------|--|--|
| Subject group type            | Reporting group  | Reporting group       |  |  |
| Number of subjects analysed   | 298              | 305                   |  |  |
| Units: percentage of subjects |                  |                       |  |  |
| number (not applicable)       |                  |                       |  |  |
| Success                       | 84.6             | 71.5                  |  |  |
| Failure                       | 15.4             | 28.5                  |  |  |

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Microbiological success                  |
| Comparison groups                       | Moxidex Solution v Moxifloxacin Solution |
| Number of subjects included in analysis | 603                                      |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.0001                                 |
| Method                                  | Chi-squared                              |

### Secondary: Percentage of subjects with treatment failure at TOC

|  |  |
|--|--|
| End point title  | Percentage of subjects with treatment failure at TOC |
| End point description:<br>Subjects who showed no clinically relevant response to the medication or who worsened in otorrhea after at least 2 full days of treatment with the study medication could be considered treatment failures. Reported as a percentage. MITT Analysis Set. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Day 15 (TOC)   |  |

| <b>End point values</b>       | Moxidex Solution | Moxifloxacin Solution |  |  |
|-------------------------------|------------------|-----------------------|--|--|
| Subject group type            | Reporting group  | Reporting group       |  |  |
| Number of subjects analysed   | 298              | 305                   |  |  |
| Units: percentage of subjects |                  |                       |  |  |
| number (not applicable)       | 6.7              | 14.8                  |  |  |

### Statistical analyses

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Treatment Failure                        |
| Comparison groups                 | Moxidex Solution v Moxifloxacin Solution |

|   |               |
|---|---------------|
| Number of subjects included in analysis | 603           |
| Analysis specification                  | Pre-specified |
| Analysis type                           | superiority   |
| P-value                                 | = 0.0015      |
| Method                                  | Chi-squared   |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All AEs 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 drug (Safety Analysis Set). Subjects were analysed based on actual treatment group.

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

### Dictionary used

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

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

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Moxidex Solution |
|-----------------------|------------------|

Reporting group description:

Subjects treated with Moxidex solution

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

Reporting group description:

Subjects treated with Moxifloxacin solution

| Serious adverse events                            | Moxidex Solution | Moxifloxacin Solution |  |
|---|------------------|-----------------------|--|
| Total subjects affected by serious adverse events |                  |                       |  |
| subjects affected / exposed                       | 0 / 389 (0.00%)  | 1 / 387 (0.26%)       |  |
| number of deaths (all causes)                     | 0                | 0                     |  |
| number of deaths resulting from adverse events    | 0                | 0                     |  |
| Infections and infestations                       |                  |                       |  |
| Cellulitis  |                  |                       |  |
| subjects affected / exposed                       | 0 / 389 (0.00%)  | 1 / 387 (0.26%)       |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1                 |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0                 |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events                            | Moxidex Solution   | Moxifloxacin Solution |  |
|---|--------------------|-----------------------|--|
| Total subjects affected by non-serious adverse events |                    |                       |  |
| subjects affected / exposed                           | 153 / 389 (39.33%) | 147 / 387 (37.98%)    |  |
| Injury, poisoning and procedural complications        |                    |                       |  |

|  |  |  |  |
|--|--|--|--|
| Injury<br>subjects affected / exposed<br>occurrences (all)   | 4 / 389 (1.03%)<br>5   | 7 / 387 (1.81%)<br>7   |  |
| General disorders and administration site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 21 / 389 (5.40%)<br>21   | 17 / 387 (4.39%)<br>17   |  |
| Ear and labyrinth disorders<br>Ear pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Otorrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Ear discomfort<br>subjects affected / exposed<br>occurrences (all) | 10 / 389 (2.57%)<br>10<br><br>8 / 389 (2.06%)<br>8<br><br>5 / 389 (1.29%)<br>5 | 12 / 387 (3.10%)<br>12<br><br>6 / 387 (1.55%)<br>7<br><br>7 / 387 (1.81%)<br>7 |  |
| Gastrointestinal disorders<br>Teething<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all)        | 13 / 389 (3.34%)<br>13<br><br>7 / 389 (1.80%)<br>7<br><br>9 / 389 (2.31%)<br>9 | 2 / 387 (0.52%)<br>2<br><br>8 / 387 (2.07%)<br>8<br><br>3 / 387 (0.78%)<br>3   |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasal congestion                                | 14 / 389 (3.60%)<br>14<br><br>12 / 389 (3.08%)<br>12                           | 13 / 387 (3.36%)<br>13<br><br>12 / 387 (3.10%)<br>12                           |  |

|   |                        |                        |  |
|---|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 5 / 389 (1.29%)<br>5   | 7 / 387 (1.81%)<br>7   |  |
| Rhinitis allergic<br>subjects affected / exposed<br>occurrences (all)                           | 2 / 389 (0.51%)<br>2   | 4 / 387 (1.03%)<br>4   |  |
| Psychiatric disorders<br>Irritability<br>subjects affected / exposed<br>occurrences (all)       | 6 / 389 (1.54%)<br>6   | 0 / 387 (0.00%)<br>0   |  |
| Infections and infestations<br>Otitis media<br>subjects affected / exposed<br>occurrences (all) | 28 / 389 (7.20%)<br>28 | 22 / 387 (5.68%)<br>22 |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)           | 25 / 389 (6.43%)<br>25 | 10 / 387 (2.58%)<br>10 |  |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                              | 7 / 389 (1.80%)<br>7   | 2 / 387 (0.52%)<br>2   |  |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 389 (0.26%)<br>1   | 5 / 387 (1.29%)<br>5   |  |
| Product issues<br>Device occlusion<br>subjects affected / exposed<br>occurrences (all)          | 3 / 389 (0.77%)<br>3   | 8 / 387 (2.07%)<br>8   |  |

## **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