



## Clinical trial results: Safety and Efficacy Evaluation of Topical Moxidex Otic Solution in the Treatment of Peri-Operative Tube Otorrhea

### Summary

EudraCT number	2018-000642-19
Trial protocol	Outside EU/EEA
Global end of trial date	11 February 2009

### Results information

Result version number	v1 (current)
This version publication date	30 July 2018
First version publication date	30 July 2018

### Trial information

#### Trial identification

Sponsor protocol code	C-05-38
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00578773
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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	11 February 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2009
Global end of trial reached?	Yes
Global end of trial date	11 February 2009
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:

The purpose of this study was to evaluate the efficacy and safety of topical Moxidex plus tympanostomy tubes (TT) for the treatment of peri-surgical tube 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	19 December 2007
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	United States: 303
Worldwide total number of subjects	303
EEA total number of subjects	0

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)	217
Children (2-11 years)	86
Adolescents (12-17 years)	0

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

## Subject disposition

### Recruitment

Recruitment details:

Subjects were recruited from 16 study centers located in the United States.

### Pre-assignment

Screening details:

This reporting group includes all enrolled and treated subjects (303).

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Investigator <sup>[1]</sup>

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Moxidex plus TT

Arm description:

Moxifloxacin 0.5%/dexamethasone phosphate 0.1% otic solution, 4 drops twice daily (BID) for 7 days, in ears with inserted tympanostomy tubes

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

Dosage and administration details:

Dosed in the affected ear(s), 4 drops twice daily (BID) for 7 days

<b>Arm title</b>	Moxifloxacin plus TT
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Arm description:

Moxifloxacin hydrochloride 0.5% solution, 4 drops BID for 7 days, in ears with inserted tympanostomy tubes

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:

Dosed in the affected ear(s), 4 drops BID for 7 days

<b>Arm title</b>	TT only
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Arm description:

Tympanostomy tube surgically inserted through the ear drum for the treatment of recurrent otitis media; no test article

Arm type	Active comparator
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Investigational medicinal product name	Tympanostomy tubes
Investigational medicinal product code	
Other name	TT
Pharmaceutical forms	Implant
Routes of administration	Auricular use
Dosage and administration details: Tubes surgically inserted through the ear drum	

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This was a single-masked trial and only the investigator was masked.

<b>Number of subjects in period 1</b>	Moxidex plus TT	Moxifloxacin plus TT	TT only
Started	100	100	103
Completed	86	85	57
Not completed	14	15	46
Treatment failure	8	9	34
Baseline culture results positive for Strep A	-	-	1
Adverse event, non-fatal	2	1	5
Baseline culture results positive for yeast	-	-	1
Subject's decision unrelated to an AE	2	1	-
Lost to follow-up	1	3	2
Tube obstruction	-	1	3
Noncompliance	1	-	-

## Baseline characteristics

### Reporting groups

Reporting group title	Moxidex plus TT
Reporting group description: Moxifloxacin 0.5%/dexamethasone phosphate 0.1% otic solution, 4 drops twice daily (BID) for 7 days, in ears with inserted tympanostomy tubes	
Reporting group title	Moxifloxacin plus TT
Reporting group description: Moxifloxacin hydrochloride 0.5% solution, 4 drops BID for 7 days, in ears with inserted tympanostomy tubes	
Reporting group title	TT only
Reporting group description: Tympanostomy tube surgically inserted through the ear drum for the treatment of recurrent otitis media; no test article	

Reporting group values	Moxidex plus TT	Moxifloxacin plus TT	TT only
Number of subjects	100	100	103
Age categorical			
This analysis population includes all subjects with successful bilateral myringotomy and TT insertion (Intent-to-Treat (ITT) Analysis Set).			
Units: Subjects			
Infants and toddlers (28 days-23 months)	82	60	75
Children (2-11 years)	18	40	28
Gender categorical			
Units: Subjects			
Female	36	37	49
Male	64	63	54

Reporting group values	Total		
Number of subjects	303		
Age categorical			
This analysis population includes all subjects with successful bilateral myringotomy and TT insertion (Intent-to-Treat (ITT) Analysis Set).			
Units: Subjects			
Infants and toddlers (28 days-23 months)	217		
Children (2-11 years)	86		
Gender categorical			
Units: Subjects			
Female	122		
Male	181		

## End points

### End points reporting groups

Reporting group title	Moxidex plus TT
Reporting group description: Moxifloxacin 0.5%/dexamethasone phosphate 0.1% otic solution, 4 drops twice daily (BID) for 7 days, in ears with inserted tympanostomy tubes	
Reporting group title	Moxifloxacin plus TT
Reporting group description: Moxifloxacin hydrochloride 0.5% solution, 4 drops BID for 7 days, in ears with inserted tympanostomy tubes	
Reporting group title	TT only
Reporting group description: Tympanostomy tube surgically inserted through the ear drum for the treatment of recurrent otitis media; no test article	

### Primary: Time (in days) to cessation of otorrhea

End point title	Time (in days) to cessation of otorrhea <sup>[1]</sup>
End point description: The time (in days) to the cessation of otorrhea (i.e. absence of otorrhea) was calculated as the number of days from surgery to the absence of otorrhea in both ears as recorded by the subject's parent/guardian via the phone-in diary. Otorrhea was defined as ending on the first day that otorrhea was absent from both ears and remaining absent for all subsequent diary entries. Pre-specified for Moxidex plus TT and TT only. ITT Analysis Set.	
End point type	Primary
End point timeframe: Up to Day 14 (Test of Cure (TOC))	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This end point was pre-specified for only 2 arms.

End point values	Moxidex plus TT	TT only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	103		
Units: Days				
median (confidence interval 95%)	1.0 (1.00 to 2.00)	4.0 (1.00 to 11.00)		

### Statistical analyses

Statistical analysis title	Time to cessation of otorrhea
Comparison groups	Moxidex plus TT v TT only

Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Logrank

## Secondary: Percentage of subjects with clinical cure at each visit

End point title	Percentage of subjects with clinical cure at each visit <sup>[2]</sup>
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End point description:

Clinical cure was defined as resolved/cured (i.e. otorrhea absent) or improved/not changed or worsened (i.e. otorrhea present) as rated by the investigator at the EOT and TOC visits. Pre-specified for Moxidex plus TT and TT only. ITT Analysis Set.

End point type	Secondary
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End point timeframe:

Day 8 (End of therapy (EOT)), Day 14 (TOC)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point was pre-specified for only 2 arms.

End point values	Moxidex plus TT	TT only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	103		
Units: percentage of subjects				
number (not applicable)				
EOT - Absent	90.0	56.3		
EOT - Present	10.0	43.7		
TOC - Absent	84.0	56.3		
TOC - Present	16.0	43.7		

## Statistical analyses

<b>Statistical analysis title</b>	Clinical Cure - EOT Absent
Comparison groups	Moxidex plus TT v TT only
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

<b>Statistical analysis title</b>	Clinical Cure - TOC Absent
Comparison groups	Moxidex plus TT v TT only



Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared

### Secondary: Percentage of subjects with microbiological outcome of success

End point title	Percentage of subjects with microbiological outcome of
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End point description:

Microbiological success (i.e. eradication of pre-therapy pathogens) was reported as a percentage. This analysis population includes all subjects in the ITT population who met pre-randomization inclusion and exclusion criteria and were culture positive for bacteria on Day 1 (Modified ITT (MITT) Analysis Set). However, any ear with a baseline culture containing Group A Streptococci or yeast or fungi were excluded from the MITT population. Pre-specified for Moxidex plus TT and TT only.

End point type	Secondary
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End point timeframe:

Day 14 (TOC)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This end point was pre-specified for only 2 arms.

End point values	Moxidex plus TT	TT only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	62		
Units: Percentage of subjects				
number (not applicable)				
Success	74.1	48.4		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects discontinued due to treatment failure

End point title	Percentage of subjects discontinued due to treatment failure <sup>[4]</sup>
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End point description:

A subject could be considered a treatment failure at the EOT, or after, if otorrhea was confirmed by an Investigator. Reported as a percentage of subjects who discontinued due to treatment failure at any point following surgery at each follow-up visit. Pre-specified for Moxidex plus TT and TT only. ITT Analysis Set.

End point type	Secondary
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End point timeframe:

Up to Day 14 (TOC)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This end point was pre-specified for only 2 arms.

<b>End point values</b>	Moxidex plus TT	TT only		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	103		
Units: percentage of subjects				
number (not applicable)	8.0	33.0		

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events 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 with successful bilateral myringotomy and TT insertion (Safety Analysis Set). Only total subjects affected by non-serious AEs that occurred at >5% are reported.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

### Reporting groups

Reporting group title	Moxidex plus TT
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Reporting group description:

Moxifloxacin 0.5%/dexamethasone phosphate 0.1% otic solution, 4 drops twice daily (BID) for 7 days plus tympanostomy tube in affected ear(s)

Reporting group title	Moxifloxacin plus TT
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Reporting group description:

Moxifloxacin hydrochloride 0.5% solution, 4 drops BID for 7 days plus tympanostomy tube in affected ear(s)

Reporting group title	TT only
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Reporting group description:

Tympanostomy tube surgically inserted through the ear drum for the treatment of recurrent otitis media; no test article

Serious adverse events	Moxidex plus TT	Moxifloxacin plus TT	TT only
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	0 / 103 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Moxidex plus TT	Moxifloxacin plus TT	TT only
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 100 (4.00%)	6 / 100 (6.00%)	6 / 103 (5.83%)
Infections and infestations			
Upper respiratory tract infection			

subjects affected / exposed	4 / 100 (4.00%)	6 / 100 (6.00%)	6 / 103 (5.83%)
occurrences (all)	4	6	6

## 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