Clinical trial results:
Safety and Efficacy Evaluation of Topical Moxidex Otic Solution in the Treatment of Acute Otitis Media with Otorrhea in Tympanostomy Tubes

Summary

EudraCT number	2018-000643-37
Trial protocol	Outside EU/EEA
Global end of trial date	14 October 2011

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-09-033

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01071902
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	14 October 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 October 2011
Global end of trial reached?	Yes
Global end of trial date	14 October 2011
Was the trial ended prematurely?	Yes

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 for the treatment of subjects with acute otitis media with tympanostomy tubes (AOMT).

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	06 April 2010
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: 345
Country: Number of subjects enrolled	Canada: 55
Worldwide total number of subjects	400
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)	177
Children (2-11 years)	220

Adolescents (12-17 years)	3
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 45 sites located in Canada (5) and the United States (40).

Pre-assignment

Screening details:

This reporting group includes all randomized subjects (400).

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
Arm title	Moxidex Solution

Arm description:

Moxifloxacin 0.5%/dexamethasone phosphate 0.1% otic solution, 4 drops twice daily (BID) for 7 days

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:

4 drops twice daily (BID) for 7 days

Arm title	Moxifloxacin Solution

Arm description:

Moxifloxacin hydrochloride 0.5% otic solution, 4 drops BID for 7 days

Arm type	Active comparator
Investigational medicinal product name	Moxifloxacin hydrochloride 0.5% otic 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

Arm title	Vehicle

Arm description:

Moxifloxacin/dexamethasone phosphate otic solution vehicle, 4 drops BID for 7 days

Arm type	Placebo
Investigational medicinal product name	Moxifloxacin/dexamethasone phosphate otic solution vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ear drops, solution
Routes of administration	Auricular use

Dosage and administration details:
4 drops BID for 7 days

Number of subjects in period 1	Moxidex Solution	Moxifloxacin Solution	Vehicle
Started	134	138	128
Completed	100	83	37
Not completed	34	55	91
Treatment failure	18	31	61
Baseline culture results positive for Strep A	2	4	2
Adverse event, non-fatal	10	16	17
Inclusion/exclusion violation	1	-	1
Baseline culture results positive for yeast	-	2	2
Lost to follow-up	1	-	-
Other - Reason not given	2	2	7
Noncompliance	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Moxidex Solution
Reporting group description:	
Moxifloxacin 0.5%/dexamethasone phosphate 0.1% otic solution, 4 drops twice daily (BID) for 7 days	
Reporting group title	Moxifloxacin Solution
Reporting group description:	
Moxifloxacin hydrochloride 0.5% otic solution, 4 drops BID for 7 days	
Reporting group title	Vehicle
Reporting group description:	
Moxifloxacin/dexamethasone phosphate otic solution vehicle, 4 drops BID for 7 days	

Reporting group values	Moxidex Solution	Moxifloxacin Solution	Vehicle
Number of subjects	134	138	128
Age categorical			
This analysis population includes all subjects who received study drug (Intent-to-Treat (ITT) Analysis Set)			
Units: Subjects			
Infants and toddlers (28 days-23 months)	62	62	53
Children (2-11 years)	72	75	73
Adolescents (12-17 years)	0	1	2
Gender categorical			
ITT Analysis Set			
Units: Subjects			
Female	54	65	52
Male	80	73	76

Reporting group values	Total		
Number of subjects	400		
Age categorical			
This analysis population includes all subjects who received study drug (Intent-to-Treat (ITT) Analysis Set)			
Units: Subjects			
Infants and toddlers (28 days-23 months)	177		
Children (2-11 years)	220		
Adolescents (12-17 years)	3		
Gender categorical			
ITT Analysis Set			
Units: Subjects			
Female	171		
Male	229		

End points

End points reporting groups

Reporting group title	Moxidex Solution
Reporting group description:	
Moxifloxacin 0.5%/dexamethasone phosphate 0.1% otic solution, 4 drops twice daily (BID) for 7 days	
Reporting group title	Moxifloxacin Solution
Reporting group description:	
Moxifloxacin hydrochloride 0.5% otic solution, 4 drops BID for 7 days	
Reporting group title	Vehicle
Reporting group description:	
Moxifloxacin/dexamethasone phosphate otic solution vehicle, 4 drops BID for 7 days	

Primary: Clinical cure rate at Day 8

End point title	Clinical cure rate at Day 8[1]

End point description:

Clinical cure was attained if the clinical response was resolved/cured (ie, absence of otorrhea) as evaluated by the Investigator at the end-of-therapy (EOT) visit. Reported as a percentage of subjects. This analysis population includes all subjects in the ITT population who were culture positive on Day 1 (Modified Intent-to-Treat (MITT) Analysis Set). Due to the study being cancelled, no statistical testing was performed.

End point type	Primary

End point timeframe:

Day 8

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed due to early termination of the study.

End point values	Moxidex Solution	Moxifloxacin Solution	Vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	91	98	
Units: percentage of subjects				
number (not applicable)	68.8	60.4	16.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cessation of Otorrhea

End point title	Time to Cessation of Otorrhea

End point description:

Time to cessation of otorrhea was defined as the time (in days) to the absence of otorrhea (i.e. otorrhea was absent and remained absent) and was calculated as the number of days from first dose of study treatment to the absence of otorrhea as recorded by parent/guardian via the patient diary. MITT with non-missing data. Due to the study being cancelled, no statistical testing was performed.

End point type	Secondary

End point timeframe:

Up to Day 8

End point values	Moxidex Solution	Moxifloxacin Solution	Vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	91	97	
Units: days				
median (full range (min-max))	3.00 (0.0 to 18.0)	4.00 (0.5 to 19.0)	6.00 (0.5 to 17.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Microbiological success at Day 8 (EOT) by Treatment

End point title	Microbiological success at Day 8 (EOT) by Treatment

End point description:

Microbiological success was defined as eradication of pre-therapy pathogens at Day 8 (EOT). A subject with no clinical signs of acute otitis media with otorrhea in tympanostomy tubes (AOMT) (i.e. clinical response was resolved/cured) and presumed eradication of pre-therapy pathogens was considered a microbiological success. Reported as a percentage. MITT Analysis Set. Due to the study being cancelled, no statistical testing was performed.

End point type	Secondary

End point timeframe:

Day 8

End point values	Moxidex Solution	Moxifloxacin Solution	Vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	91	98	
Units: percentage of subjects				
number (not applicable)	67.7	58.2	15.3	

Statistical analyses

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 who received at least one dose of study drug (Safety Analysis Set).

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

Reporting group title	Vehicle

Reporting group description:

Subjects treated with Moxidex vehicle

Serious adverse events	Moxidex Solution	Moxifloxacin Solution	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 134 (0.00%)	0 / 138 (0.00%)	0 / 128 (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: 0 %

Non-serious adverse events	Moxidex Solution	Moxifloxacin Solution	Vehicle
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 134 (32.84%)	39 / 138 (28.26%)	41 / 128 (32.03%)
Injury, poisoning and procedural complications			
Injury			
subjects affected / exposed	3 / 134 (2.24%)	1 / 138 (0.72%)	2 / 128 (1.56%)
occurrences (all)	3	1	2
Concussion			

subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
Periorbital haematoma			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
Post-traumatic pain			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Granuloma			
subjects affected / exposed	0 / 134 (0.00%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	5 / 134 (3.73%)	6 / 138 (4.35%)	3 / 128 (2.34%)
occurrences (all)	5	6	3
Malaise			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	4 / 134 (2.99%)	3 / 138 (2.17%)	1 / 128 (0.78%)
occurrences (all)	4	3	1
Ear discomfort			
subjects affected / exposed	2 / 134 (1.49%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	2	0	1
Otorrhoea			
subjects affected / exposed	0 / 134 (0.00%)	3 / 138 (2.17%)	2 / 128 (1.56%)
occurrences (all)	0	3	2
Ear haemorrhage			
subjects affected / exposed	0 / 134 (0.00%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			

subjects affected / exposed	0 / 134 (0.00%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	5 / 134 (3.73%)	2 / 138 (1.45%)	2 / 128 (1.56%)
occurrences (all)	5	2	2
Diarrhoea			
subjects affected / exposed	4 / 134 (2.99%)	1 / 138 (0.72%)	3 / 128 (2.34%)
occurrences (all)	4	1	3
Abdominal discomfort			
subjects affected / exposed	3 / 134 (2.24%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	3	0	0
Constipation			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
Teething			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	1	0	1
Oral mucosal eruption			
subjects affected / exposed	0 / 134 (0.00%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 134 (2.24%)	2 / 138 (1.45%)	2 / 128 (1.56%)
occurrences (all)	3	2	2
Nasal congestion			
subjects affected / exposed	1 / 134 (0.75%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	2	0	0
Rhinorrhoea			

subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	1	0	1
Dyspnoea			
subjects affected / exposed	0 / 134 (0.00%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 134 (0.00%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Synovial cyst			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Otitis media			
subjects affected / exposed	5 / 134 (3.73%)	10 / 138 (7.25%)	9 / 128 (7.03%)
occurrences (all)	5	10	9
Otitis media acute			
subjects affected / exposed	3 / 134 (2.24%)	6 / 138 (4.35%)	3 / 128 (2.34%)
occurrences (all)	3	6	3
Ear infection			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	2 / 128 (1.56%)
occurrences (all)	1	0	2
Otitis externa			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	2 / 128 (1.56%)
occurrences (all)	1	0	2
External ear cellulitis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	0	0	1

Folliculitis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 134 (2.24%)	1 / 138 (0.72%)	3 / 128 (2.34%)
occurrences (all)	3	1	3
Conjunctivitis			
subjects affected / exposed	2 / 134 (1.49%)	0 / 138 (0.00%)	2 / 128 (1.56%)
occurrences (all)	2	0	2
Croup infectious			
subjects affected / exposed	1 / 134 (0.75%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	1	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	3 / 128 (2.34%)
occurrences (all)	1	0	3
Sinusitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 138 (0.00%)	0 / 128 (0.00%)
occurrences (all)	1	0	0
Cellulitis			
subjects affected / exposed	0 / 134 (0.00%)	2 / 138 (1.45%)	0 / 128 (0.00%)
occurrences (all)	0	2	0
Tonsillitis			
subjects affected / exposed	0 / 134 (0.00%)	2 / 138 (1.45%)	0 / 128 (0.00%)
occurrences (all)	0	2	0
Bronchiolitis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 138 (0.72%)	0 / 128 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 138 (0.00%)	1 / 128 (0.78%)
occurrences (all)	0	0	1

Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	1 / 138 (0.72%) 1	0 / 128 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported