Clinical trial results:
Proof of Concept of Single Application of AL-60371/AL-817 Otic Suspension in Treatment of Acute Otitis Media With Tympanostomy Tubes Compared to CIPRODEX® (BID for 7 Days)

Summary

EudraCT number	2017-002689-30
Trial protocol	Outside EU/EEA
Global end of trial date	19 August 2014

Results information

Result version number	v1 (current)
This version publication date	04 January 2018
First version publication date	04 January 2018

Trial information

Trial identification

Sponsor protocol code	C-13-026

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01908803
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alcon Research Ltd
Sponsor organisation address	6201 S. Freeway, Fort Worth, Texas, United States, 76134
Public contact	Ophthalmology Unit, Novartis Pharmaceuticals , +44 0127666733391, dennis.wong@novartis.com
Scientific contact	Ophthalmology Unit, Novartis Pharmaceuticals , +44 0127666733391, dennis.wong@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	19 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 August 2014
Global end of trial reached?	Yes
Global end of trial date	19 August 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate a single application of AL-60371/AL-817 Otic Suspension relative to ototopical CIPRODEX for sustained clinical cure, microbiological success, and time to 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	26 December 2013
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: 68
Worldwide total number of subjects	68
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)	33
Children (2-11 years)	35
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 12 study centers located in the US.

Pre-assignment

Screening details:

Of the 84 enrolled, 14 subjects were exited as screen failures prior to randomization. Two randomized subjects discontinued prior to receiving investigational product.

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[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	AL-60371/AL-817

Arm description:

200 µL in affected ear(s) through tympanostomy tube on Day 1 (Visit 1)

Arm type	Experimental
Investigational medicinal product name	AL-60371/AL-817 otic suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ear drops, suspension
Routes of administration	Auricular use

Dosage and administration details:

200 µL in affected ear(s) through tympanostomy tube on Day 1 (Visit 1)

Arm title	CIPRODEX

Arm description:

Four drops in affected ear(s) twice daily through tympanostomy tube for 7 days

Arm type	Active comparator
Investigational medicinal product name	Ciprofloxacin 0.3%/dexamethasone 0.1% otic suspension
Investigational medicinal product code	
Other name	CIPRODEX®
Pharmaceutical forms	Ear drops, suspension, Ear drops, suspension
Routes of administration	Auricular use, Auricular use

Dosage and administration details:

Four drops in affected ear(s) twice daily through tympanostomy tube for 7 days

Notes:

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

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

Number of subjects in period 1	AL-60371/AL-817	CIPRODEX
Started	44	24
Completed	42	23
Not completed	2	1
Physician decision	-	1
Adverse Event	1	-
Withdrawal by Subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	AL-60371/AL-817
Reporting group description:	
200 µL in affected ear(s) through tympanostomy tube on Day 1 (Visit 1)	
Reporting group title	CIPRODEX
Reporting group description:	
Four drops in affected ear(s) twice daily through tympanostomy tube for 7 days	

Reporting group values	AL-60371/AL-817	CIPRODEX	Total
Number of subjects	44	24	68
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	2.9	2.4	
standard deviation	± 2.6	± 1.54	-
Gender categorical Units: Subjects			
Female	21	9	30
Male	23	15	38

End points

End points reporting groups	
Reporting group title	AL-60371/AL-817
Reporting group description:	
200 µL in affected ear(s) through tympanostomy tube on Day 1 (Visit 1)	
Reporting group title	CIPRODEX
Reporting group description:	
Four drops in affected ear(s) twice daily through tympanostomy tube for 7 days	

Primary: Proportion of Subjects With Sustained Clinical Cure at Day 3 Visit	
End point title	Proportion of Subjects With Sustained Clinical Cure at Day 3 Visit
End point description:	
A sustained clinical cure at Day 3 was attained if otorrhea was absent at the Day 3 visit and continued to be absent through the last study visit (Day 8 or Early Exit). Proportion of subjects is reported as a percentage. This analysis population includes all randomized subjects who received at least 1 dose of investigational product and were culture positive at the Day 1 visit in the study ear.	
End point type	Primary
End point timeframe:	
Day 3 post-treatment up to Day 8 or Early Exit	

End point values	AL-60371/AL-817	CIPRODEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	22		
Units: Percentage of subjects				
number (not applicable)	38.5	31.8		

Statistical analyses

Statistical analysis title	Sustained Clinical Cure at Day 3
Statistical analysis description:	
Descriptive statistics for the difference of the group proportions are provided including the 95% CI.	
Comparison groups	CIPRODEX v AL-60371/AL-817
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.1
upper limit	31.4

Secondary: Proportion of Subjects With Microbiological Success at the Day 8 Visit

End point title	Proportion of Subjects With Microbiological Success at the Day 8 Visit

End point description:

Microbiological success was attained if all pre-therapy bacteria were absent in the Day 8 specimen. In a subject with no otorrhea at Day 8, eradication of pre-therapy bacteria was presumed and the subject was considered a microbiological success. This analysis population includes all randomized subjects who received at least 1 dose of investigational product and were culture positive at the Day 1 visit in the study ear.

End point type	Secondary

End point timeframe:

Day 8

End point values	AL-60371/AL-817	CIPRODEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[1]	0[2]		
Units: Percentage of subjects				
arithmetic mean (standard deviation)	()	()		

Notes:

[1] - This outcome measure was not analyzed as a consequence of the study's early termination.

[2] - This outcome measure was not analyzed as a consequence of the study's early termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Median Time (in Days) to Cessation of Otorrhea

End point title	Median Time (in Days) to Cessation of Otorrhea

End point description:

Median time (in days) to the cessation of otorrhea (ie, otorrhea was absent) was calculated as the number of days from the Day 1 (Visit 1) to the absence of otorrhea in the affected ear(s) as recorded by the parent/guardian via the twice-daily diary. Cessation of otorrhea was defined as ending on the first day that otorrhea was absent from the affected ear(s) and remained absent for any/all subsequent diary entries. This analysis population includes all randomized subjects who received at least 1 dose of investigational product and were culture positive at the Day 1 visit in the study ear.

End point type	Secondary

End point timeframe:

Time to event, up to Day 8

End point values	AL-60371/AL-817	CIPRODEX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: Days				
median (standard error)	()	()		

Notes:

[3] - This outcome measure was not analyzed as a consequence of the study’s early termination.

[4] - This outcome measure was not analyzed as a consequence of the study’s early termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events (AEs) were collected for the duration of subject participation in the study (8-10 days).	
Adverse event reporting additional description:	
Only total subjects affected by non-serious AEs that occur at >5% are reported.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups	
Reporting group title	AL-60371/AL-817
Reporting group description:	
Includes all subjects administered a dose of AL-60371/AL-817	
Reporting group title	CIPRODEX
Reporting group description:	
Includes all subjects administered a dose of CIPRODEX®	

Serious adverse events	AL-60371/AL-817	CIPRODEX	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)	0 / 24 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	AL-60371/AL-817	CIPRODEX	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 44 (6.82%)	1 / 24 (4.17%)	
Infections and infestations			
Otitis media acute			
subjects affected / exposed	3 / 44 (6.82%)	1 / 24 (4.17%)	
occurrences (all)	3	2	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Terminated due to management decision.

Notes: