Clinical trial results:
OCULAR EFFECTS OF AZITHROMYCIN ORAL SOLUTION IN PEDIATRIC PATIENTS WITH PHARYNGITIS/TONSILLITIS

Summary

EudraCT number	2016-001119-19
Trial protocol	Outside EU/EEA
Global end of trial date	05 November 2015

Results information

Result version number	v2 (current)
This version publication date	10 June 2016
First version publication date	05 May 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	A0661206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01919996
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 East 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	22 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 October 2015
Global end of trial reached?	Yes
Global end of trial date	05 November 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to examine the incidence of clinically significant worsening in any of the following ophthalmic evaluations: best corrected visual activity (BCVA) (distance), color vision Farnsworth Munsell 100 Hue Test (FM-100), Amsler grid, anterior segment biomicroscopy, and dilated fundus examination, in a group of approximately 30 pediatric participants taking azithromycin oral solution for treatment of an authorized indication of use (pharyngitis/tonsillitis).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) GCP Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of study participants.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 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: 8
Worldwide total number of subjects	8
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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	8
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The sample size of 30 completed participants was specified by Food and Drug Administration (FDA) in the Post Marketing Commitment (PMC). Of the 30 pediatric participants planned for the study, 11 were screened and 8 participants received study treatment.

Pre-assignment

Screening details:

This was a prospective, non-comparative, open-label, single-arm study of azithromycin oral solution in 30 pediatric participants (aged 12 to 17 years) with pharyngitis/ tonsillitis who could be treated with azithromycin for their infection. The study design was intended to align with request from FDA to conduct the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study.

Arms

Arm title	Azithromycin

Arm description:

All participants had received open-label azithromycin oral suspension immediate release (12 mg/kg/day, up to a maximum daily dose of 500 mg) on Days 1, 2, 3, 4, and 5.

Arm type	Experimental
Investigational medicinal product name	Azithromycin
Investigational medicinal product code	CP 062993
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

All participants received azithromycin oral suspension immediate release (12 mg/kg/day, up to a maximum daily dose of 500 mg) on Days 1, 2, 3, 4 and 5.

Number of subjects in period 1	Azithromycin
Started	8
Completed	8

Baseline characteristics

Reporting groups	
Reporting group title	Azithromycin
Reporting group description:	
All participants had received open-label azithromycin oral suspension immediate release (12 mg/kg/day, up to a maximum daily dose of 500 mg) on Days 1, 2, 3, 4, and 5.	

Reporting group values	Azithromycin	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	8	8	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous | Units: Years			
arithmetic mean	14.4		
standard deviation	± 2.1	-	
Gender, Male/Female Units: Participants			
Female	6	6	
Male	2	2	

End points

End points reporting groups

Reporting group title	Azithromycin

Reporting group description:

All participants had received open-label azithromycin oral suspension immediate release (12 mg/kg/day, up to a maximum daily dose of 500 mg) on Days 1, 2, 3, 4, and 5.

Primary: Occurrence of a clinically significant worsening based on five ophthalmic examinations

End point title	Occurrence of a clinically significant worsening based on five ophthalmic examinations[1]

End point description:

Clinically significant worsening is an observed worsening in any of the five ophthalmic exams: 1) Clinically significant worsening in best corrected visual activity (BCVA) (distance) at the final visit, in either eye, is defined as a decrease in score of 5 or more letters from baseline in Early Treatment Diabetic Retinopathy Study (ETDRS) BCVA. 2) An assessment of abnormal clinically significant at final visit in color vision Farnsworth Munsell 100 Hue Test (FM-100) in either eye. 3) An assessment of abnormal clinically significant at final visit in Amsler Grid in either eye. 4) Assessments of abnormal clinically significant at final visit in anterior segment biomicroscopy, in any of the 10 eye structures in either eye. 5) Assessments of abnormal clinically significant at final visit in dilated indirect ophthalmoscopy in any of the 5 eye structures in either eye.

End point type	Primary

End point timeframe:

14 days

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 analysis was provided for the primary endpoint.

End point values	Azithromycin			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of participants				
number (not applicable)				
Clinically significant worsening - Yes	0			
Clinically significant worsening - No	87.5			
Not Evaluable	12.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of a clinically significant improvement based on five ophthalmic examinations

End point title	Occurrence of a clinically significant improvement based on five ophthalmic examinations

End point description:

1 or more of these conditions are clinically significant improvement based on five ophthalmic exams:1) clinically significant improvement in BCVA(distance) at the final visit, in either eye, defined as an

increase in score of 5 or more letters from baseline in ETDRS BCVA.2) Assessment of abnormal clinically significant at baseline and normal or abnormal, non-clinically significant at final visit in color vision(FM-100) in either eye. 3) Assessment of abnormal clinically significant at baseline and normal/abnormal, non-clinically significant at final visit in Amsler Grid in either eye. 4) Assessments of abnormal clinically significant at baseline and normal/abnormal, non-clinically significant at final visit in anterior segment biomicroscopy, in any of the 10 eye structures in either eye. 5)Assessments of abnormal clinically significant at baseline and normal/abnormal, nonclinically significant at final visit in dilated ophthalmoscopy in any of the 5 eye structures in either eye.

End point type	Secondary

End point timeframe:

14 days

End point values	Azithromycin			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of participants				
number (not applicable)				
Clinically Significant Improvement - Yes	12.5			
Clinically Significant Improvement - No	75			
Not Evaluable	12.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of a clinically significant change (improvement or worsening) based on five ophthalmic examinations

End point title	Occurrence of a clinically significant change (improvement or worsening) based on five ophthalmic examinations

End point description:

Clinically significant change (improvement or worsening) is based on five ophthalmic exams at baseline and the final visit. Any 1 or more of these conditions are a clinically significant change: 1) A worsening in BCVA (distance), as defined in outcome measure 1 OR an improvement in BCVA (distance) as defined in outcome measure 2. 2) A worsening in color vision (FM-100), as defined in outcome measure 1 OR an improvement in color vision (FM-100) as defined in outcome measure 2. 3) A worsening in Amsler Grid, as defined in outcome measure 1, OR an improvement in Amsler Grid, as defined in outcome measure 2. 4) A worsening in anterior segment biomicroscopy, as defined in outcome measure 1 OR an improvement in anterior segment biomicroscopy as defined in outcome measure 2. 5) A worsening in dilated indirect ophthalmoscopy, as defined in outcome measure 1 OR an improvement in dilated indirect ophthalmoscopy as defined in outcome measure 2.

End point type	Secondary

End point timeframe:

14 days

End point values	Azithromycin			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of participants				
number (not applicable)				
Significant Change (Improvement or Worsening-Yes	12.5			
Significant Change (Improvement or Worsening) -No	75			
Not Evaluable	12.5			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

From Day 1 up to 28 calendar days after the last administration of the study medication (up to 40 days).

Adverse event reporting additional description:

The safety population included all enrolled participants that took at least one dose of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Azithromycin

Reporting group description:

All participants had received open-label azithromycin oral suspension immediate release (12 mg/kg/day, up to a maximum daily dose of 500 mg) on Days 1, 2, 3, 4, and 5.

Serious adverse events	Azithromycin		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Azithromycin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 8 (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: There were no non-serious adverse events reported for this study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2013	Objectives and endpoints were updated to indicate that anterior segment biomicroscopy and dilated fundus examination (rather than fundus photography) were analyzed. In addition, intra-ocular pressure had been removed as an endpoint, as it does not directly support a study objective. Several statements in the inclusion criteria were considered guidance for investigators, rather than criteria. These were now sub-bullets for the respective criteria. Although culture and susceptibility testing results were not required prior to enrollment, these data were collected on the case report forms. Ophthalmologic examinations were updated to reflect detailed description of eye structures which were evaluated. Early Treatment Diabetic Retinopathy Study test instructions were included in an appendix. FM-100 Hue test description was updated to be consistent with the test manual to require 2 tests for each eye and recording of the best test results. Physical examination body systems were removed. The two lowest weight classes for children (<25 kg) were removed, as these would be below the 5th percentile for 12-year-olds. Collection of adverse event and concomitant medication information was recorded at the Day 3-5 and Day 6-13 telephone contact visits. The parent/guardian was contacted for the Day 33 telephone contact visit.

Notes:

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.

The study was terminated after the FDA released the Sponsor from the PMC. The FDA deemed the study as impracticable, given the azithromycin dose studied in the PMC was not used and the available data did not identify a signal for ocular toxicity.

Notes: