Clinical trial results:
Local, Phase IV, Multicenter, Double-blind, Randomized, Parallel, With Two Treatment Arms, Placebo-controlled Study to Evaluate the Reduction of Inflammatory Symptoms in the Treatment of Bacterial Pharyngitis With Ketoprofen And Amoxicillin in Pediatric Patients

Summary

EudraCT number	2014-004002-15
Trial protocol	Outside EU/EEA
Global end of trial date	21 June 2013

Results information

Result version number	v1 (current)
This version publication date	01 April 2016
First version publication date	28 June 2015

Trial information

Trial identification

Sponsor protocol code	KETOP_L_03102

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00799838
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi-aventis Farmacêutica Ltda
Sponsor organisation address	Avenida Major Sylvio de Magalhães Padilha, 5.200. Edifício Atlanta - Jd. Morumbi , São Paulo, Brazil, 05693-000
Public contact	Trial Transparency Team, Sanofi-aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi-aventis recherche & développement, Contact-US@sanofi.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	10 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 June 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the reduction of inflammatory signs and symptoms (hyperemia, edema and pain) after 24 hours of treatment with ketoprofen when associated with amoxicillin.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of paediatric subjects. The subject (s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. Consent form in appropriate language was explained and provided to parent(s)/guardian(s). Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2008
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	Brazil: 106
Worldwide total number of subjects	106
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)	106
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:

The study was conducted at 6 centres in Brazil. A total of 111 subjects were screened between 17 Nov 2008 and 12 June 2013.

Pre-assignment

Screening details:

Out of 111 screened subjects, 5 subjects were screen failures and 106 subjects were randomized.

Period 1

Period 1 title	Overall Study (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	Ketoprofen + Amoxicillin

Arm description:

Ketoprofen drops for 3 days along with Amoxicillin for 10 days.

Arm type	Experimental
Investigational medicinal product name	Ketoprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops, solution
Routes of administration	Oral use

Dosage and administration details:

1 drop/Kg for children aged between 4 to 6 years old or 25 drops for children from 7 to 11 years old, administered three times a day (TID).

Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

20-40 mg/Kg/day, administered TID.

Arm title	Placebo + Amoxicillin

Arm description:

Placebo (ketoprofen) drops for 3 days along with Amoxicillin for 10 days.

Arm type	Placebo
Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

20-40 mg/Kg/day, administered TID.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops, solution
Routes of administration	Oral use

Dosage and administration details:

1 drop/Kg for children aged between 4 to 6 years old or 25 drops for children from 7 to 11 years old, administered TID.

Number of subjects in period 1	Ketoprofen + Amoxicillin	Placebo + Amoxicillin
Started	51	55
Treated	51	55
Completed	48	52
Not completed	3	3
Consent withdrawal	1	-
Adverse event leading to the study withdrawal	2	2
Not attended Visit 2 at scheduled date	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Ketoprofen + Amoxicillin
Reporting group description:	
Ketoprofen drops for 3 days along with Amoxicillin for 10 days.	

Reporting group title	Placebo + Amoxicillin
Reporting group description:	
Placebo (ketoprofen) drops for 3 days along with Amoxicillin for 10 days.	

Reporting group values	Ketoprofen + Amoxicillin	Placebo + Amoxicillin	Total
Number of subjects	51	55	106
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	6.9	7.5	
standard deviation	± 2.3	± 2.2	-
Gender categorical			
Units: Subjects			
Female	27	30	57
Male	24	25	49

End points

End points reporting groups

Reporting group title	Ketoprofen + Amoxicillin

Reporting group description:

Ketoprofen drops for 3 days along with Amoxicillin for 10 days.

Reporting group title	Placebo + Amoxicillin

Reporting group description:

Placebo (ketoprofen) drops for 3 days along with Amoxicillin for 10 days.

Primary: Number of Subjects with Reduction of Inflammatory Signs and Symptoms After 24 Hours of Treatment

End point title	Number of Subjects with Reduction of Inflammatory Signs and Symptoms After 24 Hours of Treatment[1]

End point description:

Inflammatory signs and symptoms included hyperemia, edema and pain. Reduction was considered when there was an improvement in at least two of the three signs / symptoms evaluated. Analysis was performed on modified intent-to-treat (mITT) population defined as all randomized and treated subjects with available information for primary efficacy evaluation. Two subjects from "Ketoprofen + Amoxicillin" group did not have Visit 1 assessment and were excluded.

End point type	Primary

End point timeframe:

24 hours

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: As the study was prematurely terminated due to low recruitment, all analyses were performed using descriptive statistics.

End point values	Ketoprofen + Amoxicillin	Placebo + Amoxicillin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	55		
Units: subjects	40	42		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Reduction of Inflammatory Signs and Symptoms After 72 Hours of Treatment

End point title	Number of Subjects with Reduction of Inflammatory Signs and Symptoms After 72 Hours of Treatment

End point description:

Reduction of inflammatory signs and symptoms were defined in primary endpoint. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

72 hours

End point values	Ketoprofen + Amoxicillin	Placebo + Amoxicillin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	55		
Units: subjects	48	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Reduction of Inflammatory Signs and Symptoms with No Use of Rescue Medication

End point title	Number of Subjects with Reduction of Inflammatory Signs and Symptoms with No Use of Rescue Medication

End point description:

Reduction of inflammatory signs and symptoms were defined in primary endpoint. Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

24 hours and 72 hours

End point values	Ketoprofen + Amoxicillin	Placebo + Amoxicillin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	55		
Units: subjects				
24 hours	29	27		
72 hours	45	43		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Used Rescue Medication After Randomization

End point title	Number of Subjects Who Used Rescue Medication After Randomization

End point description:

Analysis was performed on mITT population.

End point type	Secondary

End point timeframe:

72 hours

End point values	Ketoprofen + Amoxicillin	Placebo + Amoxicillin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	55		
Units: subjects	18	34		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Day 10) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are AEs that developed/worsened during the study period (From the first dose of study drug up to last visit)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Ketoprofen + Amoxicillin

Reporting group description:

Ketoprofen drops for 3 days along with Amoxicillin for 10 days.

Reporting group title	Placebo + Amoxicillin

Reporting group description:

Placebo (ketoprofen) drops for 3 days along with Amoxicillin for 10 days.

Serious adverse events	Ketoprofen + Amoxicillin	Placebo + Amoxicillin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 51 (0.00%)	0 / 55 (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	Ketoprofen + Amoxicillin	Placebo + Amoxicillin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 51 (0.00%)	0 / 55 (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: Few adverse events were reported during the study period but were below the threshold of 5%

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 December 2008	- Amoxicillin dose specification was changed.
26 March 2012	- Ketoprofen study treatment duration was detailed. - Treatment kits composition was changed.
10 April 2013	- Amoxicillin treatment dosages were detailed according to the age range. - Instructions for recording the accounting of investigational products was added. - Study Population definition (mITT) was detailed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported