Clinical trial results:
Multinational, Randomized, Double Blind, Double Dummy, Comparative Study to Evaluate the Efficacy and Safety of Telithromycin Oral Suspension, 25 mg/kg Once Daily for 5 Days, Versus Penicillin V Oral Solution, 13.3 mg/kg Three Times Daily for 10 Days, in Children 6 Months to Less Than 13 Years of Age with Streptococcus Pyogenes Tonsillitis/Pharyngitis

Summary

EudraCT number	2014-004630-26
Trial protocol	Outside EU/EEA
Global end of trial date	20 September 2007

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	EFC6133, HMR3647B/3004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00315042
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sanofi U.S Services Inc.
Sponsor organisation address	55 Corporate Drive Bridgewater, New Jersey, United States, 08807
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	27 May 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 September 2007
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Primary objective of this study was to compare the bacteriologic efficacy of 5 days of telithromycin to 10 days of penicillin V in subjects with baseline bacterial throat culture positive for Streptococcus pyogenes (S. pyogenes) and repeat throat culture performed at the posttherapy/test-of-cure visit (Visit 3, Days 13 to 17) (per-protocol population for bacteriologic outcome [PPb]).

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(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. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. 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. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 March 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 314
Worldwide total number of subjects	314
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)	2
Infants and toddlers (28 days-23 months)	7
Children (2-11 years)	289
Adolescents (12-17 years)	16
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 43 sites in the United States of America. A total of 314 subjects were randomized between 12 March 2006 and 8 June 2006.

Pre-assignment

Screening details:

Of 314 randomized subjects, 305 subjects were treated.

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	Telithromycin

Arm description:

Telithromycin for 5 days.

Arm type	Experimental
Investigational medicinal product name	Telithromycin
Investigational medicinal product code	HMR3647B
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

25 mg/kg once daily.

Investigational medicinal product name	Placebo (for Penicillin V)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to penicillin V, 3 times daily for 10 day.

Arm title	Penicillin V

Arm description:

Penicillin V for 10 days.

Arm type	Active comparator
Investigational medicinal product name	Penicillin V Potassium
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

13.3 mg/kg 3 times daily.

Investigational medicinal product name	Placebo (for Telithromycin)
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to telithromycin once daily for 5 days.

Number of subjects in period 1	Telithromycin	Penicillin V
Started	155	159
Treated	150	155
Completed	126	139
Not completed	29	20
Consent withdrawn by subject	8	5
Randomized but not treated	5	4
Adverse event	7	4
Unspecified	3	5
Lost to follow-up	5	1
Lack of efficacy	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Telithromycin
Reporting group description: Telithromycin for 5 days.	
Reporting group title	Penicillin V
Reporting group description: Penicillin V for 10 days.	

Reporting group values	Telithromycin	Penicillin V	Total
Number of subjects	155	159	314
Age categorical Units: Subjects			
Newborns (0-27 days)	0	2	2
Infants and toddlers (28 days-23 months)	4	3	7
Children (2-11 years)	141	148	289
Adolescents (12-17 years)	10	6	16
Gender categorical Units: Subjects			
Female	70	79	149
Male	85	80	165

End points

End points reporting groups

Reporting group title	Telithromycin
Reporting group description: Telithromycin for 5 days.	
Reporting group title	Penicillin V
Reporting group description: Penicillin V for 10 days.	

Primary: Percentage of Subjects According to Bacteriological Outcome in Bacteriological Per Protocol (PPb) Population

End point title	Percentage of Subjects According to Bacteriological Outcome in Bacteriological Per Protocol (PPb) Population[1]

End point description:

Bacteriologic cure was defined as eradication of S. pyogenes at postbaseline culture (documented eradication). Bacteriologic failure was defined to occur if after 72 hours of study medication, a subject had a positive repeat postbaseline throat culture for S. pyogenes. The PPb population was defined as the per protocol population for analysis of bacteriologic outcome. The PPb population contained all subjects of the clinical per-protocol population (PPc) population with isolation of S. pyogenes at Visit 1 and a postbaseline culture at the Visit 3 and/or Visit 4 time window excluding the major protocol violations. Bacteriologic outcome assessment was made for the visit window in which the culture was obtained.

End point type	Primary

End point timeframe:

At posttherapy (Day 13-17)

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: This study was terminated early (randomization of 314 subjects/760 planned) the type II error was not controlled as planned and only descriptive statistics were generated.

End point values	Telithromycin	Penicillin V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	104		
Units: percentage of subjects				
number (not applicable)				
Bacteriologic Cure (Documented Eradication)	93.7	74		
Bacteriologic Failure (Documented Persistence)	6.3	26		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects According to Bacteriological Outcome in Bacteriologic Modified Intent-to-Treat (bmITT) Population

End point title	Percentage of Subjects According to Bacteriological Outcome in Bacteriologic Modified Intent-to-Treat (bmITT) Population

End point description:

Analysis was carried out on bmITT population defined as the bacteriologic modified intent to treat population that included all subjects that were in the modified intent-to-treat (mITT) population with isolation of S. pyogenes at Visit 1.

End point type	Secondary

End point timeframe:

At posttherapy (Day 13-17)

End point values	Telithromycin	Penicillin V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	135		
Units: percentage of subjects				
number (not applicable)				
Bacteriologic Cure (Documented Eradication)	80.6	64.4		
Bacteriologic Failure (Documented Persistence)	5.6	21.5		
Bacteriologic Indeterminate	13.7	14.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects According to Bacteriological Outcome in PPb Population in Late Posttherapy

End point title	Percentage of Subjects According to Bacteriological Outcome in PPb Population in Late Posttherapy

End point description:

Bacteriologic cure was defined as eradication of S. pyogenes at postbaseline culture (documented eradication).Bacteriologic failure was defined to occur if after 72 hours of study medication, a subject had a positive repeat postbaseline throat culture for S. pyogenes. Analysis was performed on PPb population. Number of subjects analysed = subjects with data available at Day 38-45.

End point type	Secondary

End point timeframe:

At late posttherapy (Day 38-45)

End point values	Telithromycin	Penicillin V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	92		
Units: percentage of subjects				
number (not applicable)				
Bacteriologic Cure (Documented Eradication)	88.8	76.1		
Bacteriologic Failure (Documented Persistence)	11.3	23.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events of Special Interest

End point title	Number of Subjects with Adverse Events of Special Interest

End point description:

Analysis was carried out on safety population which included all randomized and treated subjects.

End point type	Secondary

End point timeframe:

7 days after end of treatment

End point values	Telithromycin	Penicillin V		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	155		
Units: subjects				
Cardiac events	0	0		
Hepatic events	1	0		
Visual disturbances	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (Day 38-45) regardless of seriousness or relationship to investigational product. Analysis was performed on safety population.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (first dose of study medication and up to 7 days after the last dose of study medication or, up to 17 days after the first dose of study medication, whichever is later).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Telithromycin
Reporting group description:	
Telithromycin for 5 days.	
Reporting group title	Penicillin V
Reporting group description:	
Penicillin V for 10 days.	

Serious adverse events	Telithromycin	Penicillin V	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 150 (0.67%)	0 / 155 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 150 (0.67%)	0 / 155 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Telithromycin	Penicillin V	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 150 (7.33%)	5 / 155 (3.23%)	
Gastrointestinal disorders			

Vomiting subjects affected / exposed occurrences (all)	11 / 150 (7.33%) 11	5 / 155 (3.23%) 5	

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? Yes

Date	Interruption	Restart date
27 June 2006	In June 2006, the Sponsor voluntarily paused enrollment in pediatric clinical trials with no subsequent recruitment of subjects. On 20 September 2007, the Sponsor informed the study sites that the trial was terminated.	-

Notes:

Limitations and caveats

None reported