Clinical trial results:
A phase 1, open-label, multi-centre study to determine the PK and safety of solithromycin as add-on therapy in adolescents with suspected or confirmed bacterial infection.

Summary

EudraCT number	2014-004037-10
Trial protocol	Outside EU/EEA
Global end of trial date	05 September 2014

Results information

Result version number	v1 (current)
This version publication date	21 February 2016
First version publication date	21 February 2016

Trial information

Trial identification

Sponsor protocol code	CE01-119

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01966055
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cempra Pharmaceuticals
Sponsor organisation address	6320 Quadrangle Drive, Suite 360, Chapel Hill, United States, 27517
Public contact	Clinical Trials Info, Cempra Pharmaceuticals, clinicaltrials@cempra.com
Scientific contact	Clinical Trials Info, Cempra Pharmaceuticals, clinicaltrials@cempra.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001581-PIP01-13
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 September 2014
Global end of trial reached?	Yes
Global end of trial date	05 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Determine the PK profile of a 5-day oral dosing regimen of solithromycin

Protection of trial subjects:

Solithromycin was administered orally based on weight as add-on to antimicrobial agents administered per routine standard of care to adolescents with a suspected or confirmed infection.

Background therapy:

The most frequently used concomitant medications included sulfamethoxazole with trimethoprim, ibuprofen, ketorolac, metronidazole, multivitamins, paracetamol, and zinc sulphate.

Evidence for comparator:

Not applicable

Actual start date of recruitment	31 December 2013
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: 13
Worldwide total number of subjects	13
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)	13
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled from 6 study sites in United States.

Pre-assignment

Screening details:

1. Male or female 12 to 17 years of age (inclusive)
2. Suspected or confirmed bacterial infection with organisms against which solithromycin is expected to be active
3. No evidence or history of clinically significant medical condition
4. No diagnosis of bacterial meningitis
5.Serum creatinine < 2 mg/dL
6. Mean screening ECG QTcF < 450 ms

Period 1

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

Arms

Arm title	All subjects

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Solithromycin
Investigational medicinal product code	CEM-101
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Day 1: 12 mg/kg (not to exceed 800 mg)
Day 2: 6 mg/kg (not to exceed 400 mg/day)
The median (range) dose on Day 1 was 800 mg (400-800 mg) and on Days 2-5 was 400 mg (200-400 mg).

Number of subjects in period 1	All subjects
Started	13
Completed	13

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	13	13	
Age categorical Units: Subjects			
Adolescents (12-17 years)	13	13	
Age continuous Units: years			
arithmetic mean	15.2		
full range (min-max)	12 to 17	-	
Gender categorical Units: Subjects			
male	10	10	
female	3	3	

End points

End points reporting groups

Reporting group title	All subjects
Reporting group description: -	
Subject analysis set title	All patients
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients enrolled in the study.	

Primary: Cmin Day1

End point title	Cmin Day1[1]
End point description:	
End point type	Primary
End point timeframe:	
Day 1	

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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint..

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: microgram(s)/millilitre				
arithmetic mean (standard deviation)	0.12 (± 0.11)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax Day1

End point title	Cmax Day1[2]
End point description:	
End point type	Primary
End point timeframe:	
Day 1	

Notes:

[2] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint.

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: microgram(s)/millilitre				
arithmetic mean (standard deviation)	0.97 (± 0.73)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax Day 1

End point title	Tmax Day 1[3]

End point description:

End point type	Primary

End point timeframe:

Day1

Notes:

[3] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint.

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: hour				
arithmetic mean (standard deviation)	3.5 (± 2.1)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24 Day1

End point title	AUC0-24 Day1[4]

End point description:

End point type	Primary

End point timeframe:

Day1

Notes:

[4] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint.

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: microgram(s)/millilitre x h				
arithmetic mean (standard deviation)	11.62 (± 8.55)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-infinity Day1

End point title	AUC0-infinity Day1[5]

End point description:

End point type	Primary

End point timeframe:

Day1

Notes:

[5] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint.

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: microgram(s)/millilitre x h				
arithmetic mean (standard deviation)	14.03 (± 10.68)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmin Days 3-5

End point title	Cmin Days 3-5[6]

End point description:

End point type	Primary

End point timeframe:

Days 3-5

Notes:

[6] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint.

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: microg/mL				
arithmetic mean (standard deviation)	0.06 (± 0.08)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax Days 3-5

End point title	Cmax Days 3-5[7]

End point description:

End point type	Primary

End point timeframe:

Days 3-5

Notes:

[7] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint..

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: microgram(s)/millilitre				
arithmetic mean (standard deviation)	0.74 (± 0.61)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-24 Days 3-5

End point title	AUC0-24 Days 3-5[8]

End point description:

End point type	Primary

End point timeframe:

Days 3-5

Notes:

[8] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint..

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: microgram(s)/millilitre x h				
arithmetic mean (standard deviation)	9.28 (± 6.3)			

Statistical analyses

No statistical analyses for this end point

Primary: AUC0-infinity Days 3-5

End point title	AUC0-infinity Days 3-5[9]

End point description:

End point type	Primary

End point timeframe:

Days 3-5

Notes:

[9] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint.

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: microgram(s)/millilitre x h				
arithmetic mean (standard deviation)	10 (± 7)			

Statistical analyses

No statistical analyses for this end point

Primary: Tmax Days 3-5

End point title	Tmax Days 3-5[10]

End point description:

End point type	Primary

End point timeframe:

Days 3-5

Notes:

[10] - 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: The PK evaluation was done using a noncompartmental PK analysis (WinNonLin software version 6.3, Pharsight Corporation). There is no formal statistical analysis for this endpoint.

End point values	All patients			
Subject group type	Subject analysis set			
Number of subjects analysed	13			
Units: hour				
arithmetic mean (standard deviation)	3 (± 1.7)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first study drug administration to late follow-up visit (Day 14 +/-4).

Adverse event reporting additional description:

Every effort have been made to bring the patient back to collect concomitant medications, adverse events (AEs), and laboratory tests. If the patient was unable or unwilling to return, the concomitant medications and AEs were collected via telephone.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Safety Population

Reporting group description:

All patients who received at least 1 dose of study drug.

Serious adverse events	Safety Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Abcess limb			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 13 (61.54%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Aspartate aminotransferase increased			

subjects affected / exposed occurrences (all) Transaminases increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		
Vascular disorders Thrombophlebitis superficial subjects affected / exposed occurrences (all)	 1 / 13 (7.69%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 3 / 13 (23.08%) 3		
General disorders and administration site conditions Catheter site rash subjects affected / exposed occurrences (all)	 1 / 13 (7.69%) 1		
Ear and labyrinth disorders Middle ear effusion subjects affected / exposed occurrences (all)	 1 / 13 (7.69%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 1 / 13 (7.69%) 1		

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