Clinical trial results:
An open-label study to evaluate the penetration of doripenem in cerebrospinal fluid after doripenem administration in pediatric subjects less than 1 year chronological age

Summary

EudraCT number	2011-001114-33
Trial protocol	BE PL
Global end of trial date	02 June 2012

Results information

Result version number	v1
This version publication date	06 July 2016
First version publication date	24 July 2015

Trial information

Trial identification

Sponsor protocol code	DORIPED1002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01366651
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Archimedsweg 29-2333CM, Leiden, Netherlands,
Public contact	Clinical Registry Group, Janssen-Cilag International NV,Janssen Research & Development,
Scientific contact	Clinical Registry Group, Janssen-Cilag International NV,Janssen Research & Development,

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	03 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2012
Global end of trial reached?	Yes
Global end of trial date	02 June 2012
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to characterize the penetration of doripenem in the cerebral spinal fluid in pediatric participants less then (<1) year of age who are hospitalized and have a documented or suspected infection and are planning to, or undergoing treatment with intravenous (IV) antibiotics.

Protection of trial subjects:

Safety evaluation included following assessments: Physical examinations including body weigh ,Vital sign measurements included blood pressure, pulse rate, respiratory rate (and documentation if a participants was on a ventilator or not), and temperature (skin probe, rectal, axillary, or other) was examined.Vital signs were measured before the start of study drug infusion and within 15 minutes after the end of each doripenem infusion. Adverse events were reported throughout the study.This study was conducted in compliance with the protocol, Good Clinical Practice, and applicable regulatory requirements. A safety committee composed of the medical monitor, 1 of the study's investigators, and 1 expert in paediatrics reviewed the safety while the study was on-going.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 May 2012
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	Belgium: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	1
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
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: -

Pre-assignment

Screening details:

One participant was enrolled into the study.

Period 1

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

Arms

Arm title	Doripenem

Arm description:

Doripenem was administered as intravenous infusion for 1 hour every 8 hours at a concentration of 10 milligram per milliliter (mg/ml). The doripenem dose was 10 milligram per kilogram (mg/kg) for participants less than 12 weeks and 30 mg/kg for participants 12 weeks to less than one year of age.

Arm type	Experimental
Investigational medicinal product name	Doripenem
Investigational medicinal product code	JNJ-38174942
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Doripenem was administered as intravenous infusion for 1 hour every 8 hours at a concentration of 10 milligram per milliliter (mg/ml). Total dose was 10 milligram per kilogram (mg/kg) for participants of less than 12 weeks and 30 mg/kg for participants of 12 weeks to less than one year.

Number of subjects in period 1	Doripenem
Started	1
Completed	1

Baseline characteristics

Reporting groups	
Reporting group title	Doripenem

Reporting group description:

Doripenem was administered as intravenous infusion for 1 hour every 8 hours at a concentration of 10 milligram per milliliter (mg/ml). The doripenem dose was 10 milligram per kilogram (mg/kg) for participants less than 12 weeks and 30 mg/kg for participants 12 weeks to less than one year of age.

Reporting group values	Doripenem	Total	
Number of subjects	1	1	
Title for AgeCategorical Units: subjects			
Newborns (0-27 days)	1	1	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous Units: days			
arithmetic mean	3		
standard deviation	± 0	-	
Title for Gender Units: subjects			
Female	1	1	

End points

End points reporting groups

Reporting group title	Doripenem

Reporting group description:

Doripenem was administered as intravenous infusion for 1 hour every 8 hours at a concentration of 10 milligram per milliliter (mg/ml). The doripenem dose was 10 milligram per kilogram (mg/kg) for participants less than 12 weeks and 30 mg/kg for participants 12 weeks to less than one year of age.

Primary: Doripenem concentration in Cerebrospinal fluid

End point title	Doripenem concentration in Cerebrospinal fluid[1]

End point description:

Doripenem concentration was analyzed by validated, specific and sensitive liquid-chromatography/tandem mass spectrometry (LC-MS/MS) method.

End point type	Primary

End point timeframe:

17 minutes after end of Doripenem one hour infusion

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: Statistical analysis for this endpoint was not reported as inferential analysis was not performed as the study was terminated due to business decision.

End point values	Doripenem			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Microgram per milliliter (µg/mL)				
number (not applicable)	0.331			

Statistical analyses

No statistical analyses for this end point

Primary: Doripenem concentration in Plasma

End point title	Doripenem concentration in Plasma[2]

End point description:

Doripenem concentration was analyzed by validated, specific and sensitive liquid-chromatography/tandem mass spectrometry (LC-MS/MS) method.

End point type	Primary

End point timeframe:

10,29 minutes after end of Doripenem one hour infusion

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: Statistical analysis for this endpoint was not reported as inferential analysis was not performed as the study was terminated due to business decision.

End point values	Doripenem			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Microgram per milliliter (µg/mL)				
number (not applicable)				
10 29	26.6 24.4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Up to Day 9.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Doripenem

Reporting group description:

Doripenem was administered as intravenous infusion for 1 hour every 8 hours at a concentration of 10 milligram per milliliter (mg/ml). Total dose was 10 milligram per kilogram (mg/kg) for participants of less than 12 weeks and 30 mg/kg for participants of 12 weeks to less than one year.

Serious adverse events	Doripenem		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Doripenem		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1 (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 was no serious and non-serious adverse event in this study as the study was terminated due to business decision and is not related to any safety issues or concerns.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 October 2011	This amendment is considered to be substantial. The overall reason for the amendment is to provide clarification on a number of items and to align the protocol with recommended from investigators. It includes that the Body weight was not be collected on the day of the first doripenem infusion (Day 1). To specify the age of participants to be enrolled in days. To clarify the vital signs to be collected in the footnote of the Time & Events Schedule. To clarify the amount of time allowed between the start of the doripenem administration and the End-of-Study assessment and that CSF samples must be obtained from only a LP or VP shunt tap and that CSF sampling by other methods is not allowed. To clarify that the exclusion criteria to provide examples of the types of blood components not permitted to be administered and when. To avoid disruption of the equilibrium between plasma doripenem concentrations and CSF doripenem concentrations on study days when both samples was collected. To clarify the acceptable timeframe for eCRFs must be completed. The Centrifugation of the CSF samples is requested to avoid potential contamination of CSF with doripenem from blood components. To reduce possible physiologic variability that may confound the interpretation of pharmacokinetic data and clarification that participants should not have received an investigational compound (rather than having participated in a clinical study) within 2 weeks of the first dose of doripenem in this study. To clarify that participants with hematocrit level <30% are excluded from study participation. The timing of drawing of blood samples to match the CSF sample was clarified to avoid misunderstanding of the instructions.

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 objectives of study could not be achieved as study was terminated early on 1-july-2013 for business reasons, and is not related to any safety issues or concerns. Only 1 participant was enrolled into the study.

Notes: