Clinical trial results:
An Open-Label Study to Evaluate the Single-Dose Pharmacokinetics and Safety of Doripenem in Pediatric Subjects 6 to 17 Years of age, Inclusive, With Cystic Fibrosis

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2015-001225-16
Trial protocol	Outside EU/EEA
Global end of trial date	24 March 2010

Results information

Result version number	v2 (current)
This version publication date	02 June 2016
First version publication date	24 July 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	DORIPED1001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Johnson & Johnson Pharmaceutical Research & Development
Sponsor organisation address	Clinical Registry Group-JB BV Archimedesweg 29 , Leiden, Netherlands, 2333CM
Public contact	Clinical Registry Group-JB BV, Janssen Research and Development, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group-JB BV, Janssen Research and Development, ClinicalTrialsEU@its.jnj.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	24 March 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 March 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the pharmacokinetics of doripenem after a single administration of 30 milligram per kilogram of body weight (mg/kg) of doripenem as 4 hour intravenous (IV) infusion administered to paediatric subjects with cystic fibrosis (CF).

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety was assessed based on treatment-emergent adverse events (TEAEs), including pre-study to post-study changes in physical examination findings, vital sign measurements, and clinical laboratory analyte values. A safety committee was established to ensure that the safety of the subjects was not compromised.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 May 2009
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: 22
Worldwide total number of subjects	22
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)	10
Adolescents (12-17 years)	12
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:

Twenty-two subjects were 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

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Subjects more than or equal to (>=) 6 to less than (<) 12 years with CF who were receiving treatment with another non-study antibiotic for an infection, colonization, or prophylaxis in a hospital or supervised outpatient clinic setting were observed.

Arm type	Experimental
Investigational medicinal product name	Doripenem
Investigational medicinal product code	
Other name	Doribax
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

Subjects were given a single dose of doripenem 30 milligram per kilogram of body weight (mg/kg) for 4 hour as IV infusion.

Arm title	Group 2

Arm description:

Subjects >=12 to < 18 years with CF who were receiving treatment with another non-study antibiotic for an infection, colonization, or prophylaxis in a hospital or supervised outpatient clinic setting were observed.

Arm type	Experimental
Investigational medicinal product name	Doripenem
Investigational medicinal product code	
Other name	Doribax
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

Subjects were given a single dose of doripenem 30 mg/kg for 4 hour as IV infusion. The maximum dose of doripenem was 1000 mg.

Number of subjects in period 1	Group 1	Group 2
Started	10	12
Completed	10	10
Not completed	0	2
Adverse event, non-fatal	-	1
Other	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Subjects more than or equal to (>=) 6 to less than (<) 12 years with CF who were receiving treatment with another non-study antibiotic for an infection, colonization, or prophylaxis in a hospital or supervised outpatient clinic setting were observed.	
Reporting group title	Group 2
Reporting group description:	
Subjects >=12 to < 18 years with CF who were receiving treatment with another non-study antibiotic for an infection, colonization, or prophylaxis in a hospital or supervised outpatient clinic setting were observed.	

Reporting group values	Group 1	Group 2	Total
Number of subjects	10	12	22
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	10	0	10
Adolescents (12-17 years)	0	12	12
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	7.5	15.1	
standard deviation	± 1.35	± 1.98	-
Title for Gender			
Units: subjects			
Female	6	3	9
Male	4	9	13

End points

End points reporting groups

Reporting group title	Group 1

Reporting group description:

Subjects more than or equal to (>=) 6 to less than (<) 12 years with CF who were receiving treatment with another non-study antibiotic for an infection, colonization, or prophylaxis in a hospital or supervised outpatient clinic setting were observed.

Reporting group title	Group 2

Reporting group description:

Subjects >=12 to < 18 years with CF who were receiving treatment with another non-study antibiotic for an infection, colonization, or prophylaxis in a hospital or supervised outpatient clinic setting were observed.

Subject analysis set title	Pharmacokinetic Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pharmacokinetic analysis set included all enrolled subjects who received study drug, and had Maximum Observed Plasma Concentration (Cmax) estimation.

Primary: Maximum Observed Plasma Concentration (Cmax)

End point title	Maximum Observed Plasma Concentration (Cmax)[1]

End point description:

The Cmax is the maximum observed plasma concentration.

End point type	Primary

End point timeframe:

Pre-dose, 2.00, 4.00, 4.50, 5.00, 7.00, 9.00 hour after intravenous 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[2]	10[3]		
Units: microgram per millilitre (mcg/mL)				
arithmetic mean (standard deviation)	29 (± 9.13)	19.9 (± 3.05)		

Notes:

[2] - Pharmacokinetic Analysis Set

[3] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax)

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax)[4]

End point description:

The Tmax is defined as actual sampling time to reach maximum observed analyte concentration.

End point type	Primary

End point timeframe:

Pre-dose, 2, 4, 4.5, 5, 7, 9 hours after intravenous infusion

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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[5]	10[6]		
Units: Hour				
median (full range (min-max))	3.98 (2 to 4.18)	3.98 (2 to 4)		

Notes:

[5] - Pharmacokinetic Analysis Set

[6] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve From Time Zero to last quantifiable time (AUC[0-last])

End point title	Area Under the Plasma Concentration-Time Curve From Time Zero to last quantifiable time (AUC[0-last])[7]

End point description:

AUC (last) is area under the plasma concentration-time curve from time zero to last quantifiable time.

End point type	Primary

End point timeframe:

Pre-dose, 2, 4, 4.5, 5, 7, 9 hours after intravenous infusion

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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[8]	10[9]		
Units: microgram*hour per milliliter (mcg*h/mL)				
arithmetic mean (standard deviation)	95.6 (± 31.2)	72.7 (± 11.8)		

Notes:

[8] - Pharmacokinetic Analysis Set

[9] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity])

End point title	Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity])[10]

End point description:

The AUC (0-infinity) is the area under the plasma concentration-time curve from time zero to infinite time, calculated as the sum of AUC (last) and C (last)/lambda (z); wherein AUC(last) is area under the

plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant.

End point type	Primary

End point timeframe:

Pre-dose; 2, 4, 4.5, 5, 7, 9 hours after intravenous infusion

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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[11]	10[12]		
Units: mcg*h/ml				
arithmetic mean (standard deviation)	96.1 (± 31.7)	73 (± 11.8)		

Notes:

[11] - Pharmacokinetic Analysis Set

[12] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Decay Half-Life (t1/2)

End point title	Plasma Decay Half-Life (t1/2)[13]

End point description:

Plasma decay half-life is the time measured for the plasma concentration to decrease by one half.

End point type	Primary

End point timeframe:

Pre-dose; 2, 4, 4.5, 5, 7, 9 hours after intravenous infusion

Notes:

[13] - 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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[14]	10[15]		
Units: Hours				
arithmetic mean (standard deviation)	0.874 (± 0.159)	0.881 (± 0.0897)		

Notes:

[14] - Pharmacokinetic Analysis Set

[15] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	12.1
Reporting groups	
Reporting group title	Group 2
Reporting group description:	
Subjects who were receiving non-study antibiotic from >=12 years to <18 years of age was observed.	
Reporting group title	Group 1
Reporting group description:	
Subjects who were receiving non-study antibiotic from more than or equal to (>=) 6 years to less than (<) 12 years of age was observed.	

Serious adverse events	Group 2	Group 1	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Group 2	Group 1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 12 (50.00%)	7 / 10 (70.00%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood Bilirubin Increased			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood Creatinine Increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pallor			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Application Site Erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Application Site Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Application Site Vesicles			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Infusion Site Erythema			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Infusion Site Extravasation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Infusion Site Irritation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Abdominal Discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Pain in Extremity			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2009	Protocol amendment 1 included revision of inclusion criterion to allow the flexibility to enroll subjects receiving antibiotic therapy outside the hospital and also for the subjects receiving antibiotics without an IV catheter in place. Withdrawal criterion for interrupted doripenem infusion was modified from interruption more than 5 minutes to more than 10 minutes.
22 June 2009	Protocol amendment 2 included withdrawal from study was modified to allow re-enrollment of subjects withdrawn for reasons other than safety. Instructions regarding pharmacokinetic sample collection in the cases where study drug administration could have been interrupted for less than or equal to 10 minutes were clarified.
01 October 2009	Protocol amendment 3 deleted an inclusion criterion for weight requirement (within the 5th and the 95th percentile), to allow enrollment of subjects with lower body weight. Study withdrawal section and dosage and administration section were updated to clarify that the subject was to be withdrawn if the total interruption in study drug administration occurred for more than 10 minutes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported