Clinical trial results:
An Open-Label, Parallel-Group Study to Evaluate the Single-Dose Pharmacokinetics and Safety of Doripenem in Pediatric Patients 3 Months to 17 Years of Age, Inclusive

Summary

EudraCT number	2011-005159-15
Trial protocol	Outside EU/EEA
Global end of trial date	21 November 2008

Results information

Result version number	v2 (current)
This version publication date	02 June 2016
First version publication date	08 August 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	DORI-NOS-1008

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, L.L.C.
Sponsor organisation address	Raritan, 920 Route 202, New Jersey, United States,
Public contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International NV, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000015-PIP01-07
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	21 November 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 November 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the pharmacokinetics of doripenem and its metabolite, doripenem-M-1, in pediatric subjects 3 months to 17 years of age, inclusive.

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 throughout the study by monitoring adverse events, conducting clinical laboratory tests (hematology, serum chemistry, and urinalysis), pregnancy test, vital signs (temperature, pulse, respiratory rate, and blood pressure), physical examination (height/length and weight), and recording concomitant medications.The study protocol and amendment were reviewed by an Institutional Review Board (IRB).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 July 2007
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: 50
Worldwide total number of subjects	50
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)	12
Children (2-11 years)	26

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:

A total of 50 pediatric participants (boys and girls) 3 months to 17 years of age inclusive, were planned to be enrolled in this 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	>= 12 to <18 yr

Arm description:

Subjects from age group (greater than or equal to [>=] 12 years to less than [<]18 years) received doripenem 15 milligram per kilogram (mg/kg) (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter.

Arm type	Experimental
Investigational medicinal product name	Doripenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravascular use

Dosage and administration details:

Subjects from age group (>=12 years to <18 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter.

Arm title	>=6 to <12yr

Arm description:

Subjects from age group (>=6 years to <12 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter

Arm type	Experimental
Investigational medicinal product name	Doripenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects from age group (>=6 years to <12 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter.

Arm title	>=2 to <6 yr

Arm description:

Subjects from age group (>=2 years to <6 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter

Arm type	Experimental

Investigational medicinal product name	Doripenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects from age group (>=2 years to <6 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter.

Arm title	>=3 mon to <2 yr

Arm description:

Subjects from age group (>=3 months to <2 years) received 10 mg/kg doripenem as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter

Arm type	Experimental
Investigational medicinal product name	Doripenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravascular use

Dosage and administration details:

Subjects from age group (>=3 months to <2 years) received 10 mg/kg doripenem as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter.

Number of subjects in period 1	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr
Started	12	13	13
Completed	11	11	13
Not completed	1	2	0
Adverse event, non-fatal	-	1	-
Other	1	1	-

Number of subjects in period 1	>=3 mon to <2 yr
Started	12
Completed	12
Not completed	0
Adverse event, non-fatal	-
Other	-

Baseline characteristics

Reporting groups	
Reporting group title	>= 12 to <18 yr
Reporting group description:	
Subjects from age group (greater than or equal to [>=] 12 years to less than [<]18 years) received doripenem 15 milligram per kilogram (mg/kg) (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter.	
Reporting group title	>=6 to <12yr
Reporting group description:	
Subjects from age group (>=6 years to <12 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter	
Reporting group title	>=2 to <6 yr
Reporting group description:	
Subjects from age group (>=2 years to <6 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter	
Reporting group title	>=3 mon to <2 yr
Reporting group description:	
Subjects from age group (>=3 months to <2 years) received 10 mg/kg doripenem as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter	

Reporting group values	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr
Number of subjects	12	13	13
Title for AgeCategorical			
Units: subjects			
infants and toddlers(28 days-23 months)	0	0	0
Children (2-11 years)	0	13	13
Adolescents (12-17 years)	12	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	14.8	8.7	4.1
standard deviation	± 1.04	± 2.09	± 1.31
Title for Gender			
Units: subjects			
Female	5	5	8
Male	7	8	5

Reporting group values	>=3 mon to <2 yr	Total	
Number of subjects	12	50	
Title for AgeCategorical			
Units: subjects			
infants and toddlers(28 days-23 months)	12	12	
Children (2-11 years)	0	26	
Adolescents (12-17 years)	0	12	
Title for AgeContinuous			
Units: years			
arithmetic mean	1.2		

standard deviation	± 0.65	-	

Title for Gender Units: subjects			
Female	6	24	
Male	6	26	

End points

End points reporting groups

Reporting group title	>= 12 to <18 yr

Reporting group description:

Subjects from age group (greater than or equal to [>=] 12 years to less than [<]18 years) received doripenem 15 milligram per kilogram (mg/kg) (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter.

Reporting group title	>=6 to <12yr

Reporting group description:

Subjects from age group (>=6 years to <12 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter

Reporting group title	>=2 to <6 yr

Reporting group description:

Subjects from age group (>=2 years to <6 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter

Reporting group title	>=3 mon to <2 yr

Reporting group description:

Subjects from age group (>=3 months to <2 years) received 10 mg/kg doripenem as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter

Primary: Maximum Observed Plasma Concentration (Cmax) of Doripenem

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

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour (hr) post dose

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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[2]	10[3]	13[4]	12[5]
Units: Microgram per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	18.9 (± 5.9)	29.1 (± 6.34)	26.1 (± 3.02)	16.7 (± 4.43)

Notes:

[2] - Pharmacokinetic Analysis Set

[3] - Pharmacokinetic Analysis Set

[4] - Pharmacokinetic Analysis Set

[5] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

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

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) of Doripenem[6]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

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

End point values	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[7]	10[8]	13[9]	12[10]
Units: Hour				
median (full range (min-max))	0.98 (0.52 to 1.13)	1 (0.5 to 1.1)	1 (0.92 to 1.02)	1 (0.97 to 1.5)

Notes:

[7] - Pharmacokinetic Analysis Set

[8] - Pharmacokinetic Analysis Set

[9] - Pharmacokinetic Analysis Set

[10] - 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]) of Doripenem

End point title	Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Doripenem[11]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[11] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[12]	11[13]	12[14]	12[15]
Units: Microgram.hour per milliliter(mcg.hr/mL)				
arithmetic mean (standard deviation)	31.1 (± 6.13)	44.8 (± 11.1)	40.6 (± 8.47)	29.8 (± 10.2)

Notes:

[12] - Pharmacokinetic Analysis Set

[13] - Pharmacokinetic Analysis Set

[14] - Pharmacokinetic Analysis Set

[15] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Elimination Half-Life (t1/2) of Doripenem

End point title	Plasma Elimination Half-Life (t1/2) of Doripenem[16]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[16] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[17]	11[18]	12[19]	12[20]
Units: Hour				
arithmetic mean (standard deviation)	0.944 (± 0.225)	0.919 (± 0.211)	0.937 (± 0.355)	1.01 (± 0.426)

Notes:

[17] - Pharmacokinetic Analysis Set

[18] - Pharmacokinetic Analysis Set

[19] - Pharmacokinetic Analysis Set

[20] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Volume of Distribution (Vdss) of Doripenem

End point title	Apparent Volume of Distribution (Vdss) of Doripenem[21]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[21] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[22]	11[23]	12[24]	12[25]
Units: Liter				
arithmetic mean (standard deviation)	17.8 (± 4.71)	10.6 (± 4.38)	6.34 (± 1.32)	4.86 (± 3.56)

Notes:

[22] - Pharmacokinetic Analysis Set

[23] - Pharmacokinetic Analysis Set

[24] - Pharmacokinetic Analysis Set

[25] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Systemic Clearance (CL) of Doripenem

End point title	Systemic Clearance (CL) of Doripenem[26]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[26] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[27]	11[28]	12[29]	12[30]
Units: Liter per hour (L/h)				
arithmetic mean (standard deviation)	16.7 (± 3.6)	10.5 (± 4.78)	6.29 (± 1.62)	3.88 (± 1.67)

Notes:

[27] - Pharmacokinetic Analysis Set

[28] - Pharmacokinetic Analysis Set

[29] - Pharmacokinetic Analysis Set

[30] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Renal Clearance (CLr) of Doripenem

End point title	Renal Clearance (CLr) of Doripenem[31]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[31] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[32]	8[33]	9[34]	11[35]
Units: Liter per hour (L/h)				
arithmetic mean (standard deviation)	12.4 (± 5.78)	6.8 (± 1.68)	3.33 (± 2)	2.18 (± 3.02)

Notes:

[32] - Pharmacokinetic Analysis Set

[33] - Pharmacokinetic Analysis Set

[34] - Pharmacokinetic Analysis Set

[35] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Creatinine clearance [CLcr] of Doripenem

End point title	Creatinine clearance [CLcr] of Doripenem[36]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[36] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[37]	11[38]	10[39]	11[40]
Units: mL/min/kg				
arithmetic mean (standard deviation)	3.06 (± 0.77)	5.52 (± 1.94)	11.3 (± 7.84)	16.6 (± 8.63)

Notes:

[37] - Pharmacokinetic Analysis Set

[38] - Pharmacokinetic Analysis Set

[39] - Pharmacokinetic Analysis Set

[40] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Total amount excreted into urine [Ae] of Doripenem

End point title	Total amount excreted into urine [Ae] of Doripenem[41]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[41] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[42]	8[43]	9[44]	11[45]
Units: percent, dose (%,dose)				
arithmetic mean (standard deviation)	74.4 (± 24.9)	72.4 (± 24.5)	48.1 (± 24.8)	50.6 (± 50)

Notes:

[42] - Pharmacokinetic Analysis Set

[43] - Pharmacokinetic Analysis Set

[44] - Pharmacokinetic Analysis Set

[45] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) of Metabolite Doripenem-M-1

End point title	Maximum Observed Plasma Concentration (Cmax) of Metabolite Doripenem-M-1[46]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[46] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[47]	11[48]	13[49]	12[50]
Units: Microgram per milliliter (mcg/mL)				
arithmetic mean (standard deviation)	2.15 (± 0.82)	3.15 (± 1.81)	2.7 (± 0.92)	1.73 (± 0.856)

Notes:

[47] - Pharmacokinetic Analysis Set

[48] - Pharmacokinetic Analysis Set

[49] - Pharmacokinetic Analysis Set

[50] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Metabolite Doripenem-M-1

End point title	Time to Reach Maximum Observed Plasma Concentration (Tmax) of Metabolite Doripenem-M-1[51]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[51] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[52]	10[53]	13[54]	12[55]
Units: Hour				
median (full range (min-max))	0.98 (0.52 to 1.48)	1.01 (0.97 to 1.1)	1 (0.92 to 1.02)	1 (0.97 to 2)

Notes:

[52] - Pharmacokinetic Analysis Set

[53] - Pharmacokinetic Analysis Set

[54] - Pharmacokinetic Analysis Set

[55] - 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]) ofInfinite Time (AUC[0-infinity]) of Metabolite Doripenem-M-1

End point title	Area Under the Plasma Concentration-Time Curve From Time Zero to Infinite Time (AUC[0-infinity]) ofInfinite Time (AUC[0-infinity]) of Metabolite Doripenem-M-1[56]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[56] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[57]	11[58]	13[59]	12[60]
Units: Microgram.hour per				
arithmetic mean (standard deviation)	5.07 (± 1.55)	6.48 (± 2.02)	6.28 (± 2.38)	4.89 (± 2.98)

Notes:

[57] - Pharmacokinetic Analysis Set

[58] - Pharmacokinetic Analysis Set

[59] - Pharmacokinetic Analysis Set

[60] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Elimination Half-Life (t1/2) of Metabolite Doripenem-M-1

End point title	Plasma Elimination Half-Life (t1/2) of Metabolite Doripenem-M-1[61]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[61] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[62]	11[63]	13[64]	12[65]
Units: Hour				
arithmetic mean (standard deviation)	1.76 (± 0.369)	1.55 (± 0.465)	1.61 (± 0.743)	1.61 (± 0.47)

Notes:

[62] - Pharmacokinetic Analysis Set

[63] - Pharmacokinetic Analysis Set

[64] - Pharmacokinetic Analysis Set

[65] - Pharmacokinetic Analysis Set

Statistical analyses

No statistical analyses for this end point

Primary: Total amount excreted into urine [Ae] of Metabolite Doripenem-M-1

End point title	Total amount excreted into urine [Ae] of Metabolite Doripenem-M-1[66]

End point description:

End point type	Primary

End point timeframe:

Up to 8 hour post dose

Notes:

[66] - 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	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr	>=3 mon to <2 yr
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10[67]	8[68]	8[69]	11[70]
Units: percent, dose (%,dose)				
arithmetic mean (standard deviation)	11.8 (± 5.3)	12.8 (± 3.76)	8.76 (± 2.78)	10.2 (± 12.2)

Notes:

[67] - Pharmacokinetic Analysis Set

[68] - Pharmacokinetic Analysis Set

[69] - Pharmacokinetic Analysis Set

[70] - 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	11.1

Reporting groups	
Reporting group title	>= 12 to <18 yr
Reporting group description:	
Subjects from age group (>=12 years to <18 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter	
Reporting group title	>=6 to <12yr
Reporting group description:	
Subjects from age group (>=6 years to <12 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter	
Reporting group title	>=2 to <6 yr
Reporting group description:	
Subjects from age group (>=2 years to <6 years) received doripenem 15 mg/kg (approximately equivalent to 1,000 mg/70 kg adult) as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter	
Reporting group title	>=3 mon to <2 yr
Reporting group description:	
Subjects from age group (>=3 months to <2 years) received 10 mg/kg doripenem as an i.v. infusion (5 mg/mL infusion solution) over 1 hour via an indwelling catheter	

Serious adverse events	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	2 / 13 (15.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Surgical and medical procedures			
Abscess Drainage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central Venous Catheterisation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	>=3 mon to <2 yr		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Surgical and medical procedures			
Abscess Drainage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Central Venous Catheterisation			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	>= 12 to <18 yr	>=6 to <12yr	>=2 to <6 yr
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	7 / 13 (53.85%)	9 / 13 (69.23%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Drug Withdrawal Syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pyrexia			

subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Suprapubic Pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pleural Effusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Pulmonary Oedema			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Respiratory Distress			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Mental Status Changes			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood Potassium Increased			

subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood Pressure Increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Cardiac Murmur			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Creatinine Urine Increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Eosinophil Count Increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Crystal Urine Present			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	2 / 12 (16.67%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	2	1	0
Haematocrit Decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Haemoglobin Decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Heart Rate Increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Oxygen Saturation Decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Protein Urine Present			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Protein S Increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Urine Ketone Body Present			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Cardiac disorders			
Cardiac Failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Pericardial Effusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Dizziness Postural			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Middle Ear Effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal Pain			

subjects affected / exposed	1 / 12 (8.33%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	2 / 13 (15.38%)
occurrences (all)	1	0	2
Tongue Disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	3 / 13 (23.08%)
occurrences (all)	0	2	3
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	1 / 13 (7.69%)
occurrences (all)	0	1	1
Renal and urinary disorders			
Crystalluria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Ketonuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Oral Candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Skin Infection			

subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Hypovolaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	>=3 mon to <2 yr		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest Discomfort			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Drug Withdrawal Syndrome			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Suprapubic Pain			

subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pleural Effusion			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pulmonary Oedema			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Respiratory Distress			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Psychiatric disorders			
Mental Status Changes			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood Potassium Increased			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Blood Pressure Increased			

subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Cardiac Murmur				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Creatinine Urine Increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Eosinophil Count Increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Crystal Urine Present				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Gamma-Glutamyltransferase Increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Haematocrit Decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Haemoglobin Decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Heart Rate Increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Oxygen Saturation Decreased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Protein Urine Present				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			
Protein S Increased				
subjects affected / exposed	0 / 12 (0.00%)			
occurrences (all)	0			

Urine Ketone Body Present subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Cardiac disorders Cardiac Failure subjects affected / exposed occurrences (all) Pericardial Effusion subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Dizziness Postural subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0		
Ear and labyrinth disorders Middle Ear Effusion subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0		
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all) Constipation	 0 / 12 (0.00%) 0 		

subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Tongue Disorder subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0 1 / 12 (8.33%) 1 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Renal and urinary disorders Crystalluria subjects affected / exposed occurrences (all) Ketonuria subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Infections and infestations Oral Candidiasis subjects affected / exposed occurrences (all) Skin Infection subjects affected / exposed occurrences (all)	 0 / 12 (0.00%) 0 0 / 12 (0.00%) 0		
Metabolism and nutrition disorders			

Decreased Appetite subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Hyperphosphataemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Hypovolaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 July 2008	The major reasons for amendments to the original protocol includes at least 5 participants were to be enrolled in the youngest age group instead of 4 participants, upon completion of enrollment for each age group, interim pharmacokinetic analysis was performed to assess preliminary exposure of participants to doripenem, language was updated throughout protocol to reflect incorporation of interim analysis and to state that "study conclusions will be based on the final pharmacokinetic analysis after enrollment of all participants across all age cohorts.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported