



Clinical trial results:

A Prospective, Randomized, Double-Blind, Multicenter Study to Establish the Safety and Tolerability of Doripenem Compared With Meropenem in Hospitalized Children With Complicated Intra-Abdominal Infections.

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

Summary

EudraCT number	2009-015864-32
Trial protocol	LT LV Outside EU/EEA
Global end of trial date	09 September 2013

Results information

Result version number	v2 (current)
This version publication date	09 June 2016
First version publication date	23 July 2015
Version creation reason	- Correction of full data set - Review of data

Trial information

Trial identification

Sponsor protocol code	DORIPED3001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01110382
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Turnhoutseweg 30, 2340 Beerse , Belgium, Belgium,
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)	EMA-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	09 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 September 2013
Global end of trial reached?	Yes
Global end of trial date	09 September 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to establish the safety and tolerability profile of doripenem compared with that of meropenem in hospitalized children 3 months to less than 18 years of age with cIAI (complicated intra-abdominal infection).

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. An Independent Data Monitoring Committee [IDMC] monitored the safety of participants in this study as well as 2 additional Phase 3 paediatric trials being conducted by the Sponsor simultaneously. Safety evaluations included the measurement of vital signs, monitoring of reported adverse effects (AEs), including serious adverse effects (SAEs), concomitant therapy, serum chemistry, hematology assessments, and urinalysis with microscopy.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2010
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	Argentina: 4
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	Lithuania: 10
Country: Number of subjects enrolled	Latvia: 6
Country: Number of subjects enrolled	Panama: 5
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	41
EEA total number of subjects	16

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)	30
Adolescents (12-17 years)	11
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:

Of the 41 participants, 31 participants were assigned to treatment with doripenem and 10 participants were assigned to treatment with meropenem.

Period 1

Period 1 title	Overall (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	Doripenem

Arm description:

Doripenem 20 milligram per kilogram [mg/kg] per dose (up to 500 milligram per dose [mg/dose]) was administered every 8 hours as 60-minutes intravenous [IV] (at least 3 days of IV doripenem only or IV doripenem followed by oral amoxicillin/clavulanate potassium). Total duration of treatment 10 to 14 days.

Arm type	Experimental
Investigational medicinal product name	Doripenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Doripenem 20 milligram per kilogram [mg/kg] per dose (up to 500 milligram per dose [mg/dose]) was administered every 8 hours as 60-minutes intravenous [IV] (at least 3 days of IV doripenem only or IV doripenem followed by oral amoxicillin/clavulanate potassium).

Arm title	Meropenem
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Arm description:

Meropenem 20 milligram per kilogram [mg/kg] per dose (up to 1 gram per dose [g/dose]) was administered every 8 hours as 30-minutes intravenous [IV] (at least 3 days of IV meropenem only or IV meropenem followed by oral amoxicillin/clavulanate potassium). Total duration of treatment 10 to 14 days.

Arm type	Active comparator
Investigational medicinal product name	Meropenem
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Meropenem 20 milligram per kilogram [mg/kg] per dose (up to 1 gram per dose [g/dose]) was administered every 8 hours as 30-minutes intravenous [IV] (at least 3 days of IV meropenem only or IV meropenem followed by oral amoxicillin/clavulanate potassium).

Number of subjects in period 1	Doripenem	Meropenem
Started	31	10
Completed	31	8
Not completed	0	2
Consent withdrawn by subject	-	1
Other	-	1

Baseline characteristics

Reporting groups

Reporting group title	Doripenem
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Reporting group description:

Doripenem 20 milligram per kilogram [mg/kg] per dose (up to 500 milligram per dose [mg/dose]) was administered every 8 hours as 60-minutes intravenous [IV] (at least 3 days of IV doripenem only or IV doripenem followed by oral amoxicillin/clavulanate potassium). Total duration of treatment 10 to 14 days.

Reporting group title	Meropenem
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Reporting group description:

Meropenem 20 milligram per kilogram [mg/kg] per dose (up to 1 gram per dose [g/dose]) was administered every 8 hours as 30-minutes intravenous [IV] (at least 3 days of IV meropenem only or IV meropenem followed by oral amoxicillin/clavulanate potassium). Total duration of treatment 10 to 14 days.

Reporting group values	Doripenem	Meropenem	Total
Number of subjects	31	10	41
Title for AgeCategorical Units: subjects			
Children (2-11 years)	23	7	30
Adolescents (12-17 years)	8	3	11
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	8.5	9.3	
standard deviation	± 3.4	± 4.52	-
Title for Gender Units: subjects			
Female	15	0	15
Male	16	10	26

End points

End points reporting groups

Reporting group title	Doripenem
Reporting group description: Doripenem 20 milligram per kilogram [mg/kg] per dose (up to 500 milligram per dose [mg/dose]) was administered every 8 hours as 60-minutes intravenous [IV] (at least 3 days of IV doripenem only or IV doripenem followed by oral amoxicillin/clavulanate potassium). Total duration of treatment 10 to 14 days.	
Reporting group title	Meropenem
Reporting group description: Meropenem 20 milligram per kilogram [mg/kg] per dose (up to 1 gram per dose [g/dose]) was administered every 8 hours as 30-minutes intravenous [IV] (at least 3 days of IV meropenem only or IV meropenem followed by oral amoxicillin/clavulanate potassium). Total duration of treatment 10 to 14 days.	
Subject analysis set title	Clinical Intent-to-Treat (CITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: All randomized participants who met the minimal disease definition of complicated intra-abdominal infection regardless if a baseline pathogen was isolated from the intra-abdominal cavity.	
Subject analysis set title	Microbiological intent-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: Participants of CITT with at least 1 baseline bacterial pathogen isolated from the intra-abdominal cavity that was susceptible to both doripenem and meropenem. 8 and 2 participants from doripenem and meropenem, respectively had no susceptible intra-abdominal pathogen at baseline and were excluded from this set.	

Primary: The Number of Participants With Clinical Cure Rate at Test Of Cure (TOC) Visit

End point title	The Number of Participants With Clinical Cure Rate at Test Of Cure (TOC) Visit
End point description: The participants were considered as clinical cure if they had clinical improvement in signs and symptoms of the intra-abdominal infection such that no additional antibacterial therapy or surgical or percutaneous intervention is/was required for the treatment of the index infection, no fever, and a favourable response at End of IV visit.	
End point type	Primary
End point timeframe: TOC (7 to 14 days after the last dose of study medication therapy)	

End point values	Doripenem	Meropenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31 ^[1]	10 ^[2]		
Units: Participants				
number (not applicable)	23	7		

Notes:

[1] - Clinical Intent-to-Treat (CITT)

[2] - Clinical Intent-to-Treat (CITT)

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Doripenem v Meropenem
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other ^[3]
Parameter estimate	Difference clinical cure rates (%)
Point estimate	4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.7
upper limit	43.1

Notes:

[3] - Descriptive study.

Secondary: The Number of Participants With Clinical Improvement Rate at End of IV (EIV) Visit

End point title	The Number of Participants With Clinical Improvement Rate at End of IV (EIV) Visit
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End point description:

The participants were considered as clinical improved if they had clinical improvement in signs and symptoms of the intra-abdominal infection, no fever, decrease in white blood cell (WBC) , and not received any non study antibiotics for the treatment of intra-abdominal infection after IV study drug therapy had begun period at the end.

End point type	Secondary
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End point timeframe:

EIV (within 24 hours after completion of the last dose of IV study medication therapy)

End point values	Doripenem	Meropenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31 ^[4]	10 ^[5]		
Units: Participants				
number (not applicable)	29	8		

Notes:

[4] - Clinical Intent-to-Treat (CITT)

[5] - Clinical Intent-to-Treat (CITT)

Statistical analyses

Statistical analysis title	Statistical analysis 2
Comparison groups	Doripenem v Meropenem
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other ^[6]
Parameter estimate	Difference clinical improvement rates(%)
Point estimate	13.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.3
upper limit	46.4

Notes:

[6] - Descriptive study.

Secondary: The Number of Participants With Clinical Cure Rate at Late Follow-Up (LFU) Visit

End point title	The Number of Participants With Clinical Cure Rate at Late Follow-Up (LFU) Visit
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End point description:

The participants were considered as clinical cure if they had clinical improvement in signs and symptoms of the intra-abdominal infection such that no additional antibacterial therapy or surgical or percutaneous intervention is/was required for the treatment of the index infection, no fever, and a favourable response at End of IV visit.

End point type	Secondary
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End point timeframe:

LFU (28 to 42 days after the last dose of study medication therapy)

End point values	Doripenem	Meropenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31 ^[7]	10 ^[8]		
Units: Participants				
number (not applicable)	22	6		

Notes:

[7] - Clinical Intent-to-Treat (CITT)

[8] - Clinical Intent-to-Treat (CITT)

Statistical analyses

Statistical analysis title	Statistical analysis 3
Comparison groups	Doripenem v Meropenem
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	other ^[9]
Parameter estimate	Difference Clinical Cure Rate (%)
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30
upper limit	51.9

Notes:

[9] - Descriptive study.

Secondary: The Number of Participants With Favorable Per-participant Microbiological Response

End point title	The Number of Participants With Favorable Per-participant Microbiological Response
End point description: Favourable per-participant microbiological response rate was evaluated at the at End of IV (EIV) visit, Test Of Cure (TOC) visit, and Late Follow-Up (LFU) visit. The favourable per-participant microbiological response was considered when all baseline pathogens were eradicated (absence) or presumed eradicated (absence of material to culture in a participant who has a positive clinical response to treatment).	
End point type	Secondary
End point timeframe: EIV (within 24 hours after completion of the last dose of IV study medication therapy), TOC (7 to 14 days after the last dose of study medication therapy), and LFU (28 to 42 days after the last dose of study medication therapy)	

End point values	Doripenem	Meropenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23 ^[10]	8 ^[11]		
Units: Participants				
number (not applicable)				
EIV visit	21	6		
TOC visit	17	5		
LFU visit	17	5		

Notes:

[10] - Microbiological intent-to-treat

[11] - Microbiological intent-to-treat

Statistical analyses

Statistical analysis title	Favorable Microbiological Response (MR) at EIV.
Comparison groups	Doripenem v Meropenem
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other ^[12]
Parameter estimate	Difference between MR rate (%)
Point estimate	16.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.3
upper limit	56.9

Notes:

[12] - Descriptive study.

Statistical analysis title	Favorable Microbiological Response (MR) at TOC.
Comparison groups	Doripenem v Meropenem

Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other ^[13]
Parameter estimate	Difference between MR rate (%)
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.1
upper limit	57.9

Notes:

[13] - Descriptive study.

Statistical analysis title	Favorable Microbiological Response (MR) at LFU
Comparison groups	Doripenem v Meropenem
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	other ^[14]
Parameter estimate	Difference between MR rate (%)
Point estimate	11.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.1
upper limit	57.9

Notes:

[14] - Descriptive study.

Secondary: Number of Participants With Favorable Per-pathogen Microbiological Outcome Rate at End of IV (EIV) Visit

End point title	Number of Participants With Favorable Per-pathogen Microbiological Outcome Rate at End of IV (EIV) Visit
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End point description:

A total of 24 pathogens in the doripenem group and 6 pathogens in the meropenem group were isolated at baseline from the intra-abdominal culture and were susceptible to the study drug received. The most common pathogens isolated from the intra-abdominal culture are listed in the table below; the numbers in parenthesis next to each pathogen represent the number of participants with the pathogen isolated at baseline in the doripenem and meropenem treatment groups, respectively. The favorable per-pathogen microbiological outcome was considered when all baseline pathogens were eradicated (absence) or presumed eradicated (absence of material to culture in a participant who has a positive clinical response to treatment).

End point type	Secondary
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End point timeframe:

EIV (within 24 hours after completion of the last dose of IV study medication therapy)

End point values	Doripenem	Meropenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23 ^[15]	8 ^[16]		
Units: Participants				
number (not applicable)				
Streptococcus anginosus (n=13, 0)	12	0		
Escherichia coli (n=19, 8)	18	6		
Bacteroides fragilis (n=11, 1)	10	1		

Notes:

[15] - Microbiological intent-to-treat

[16] - Microbiological intent-to-treat

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Favorable Per-pathogen Microbiological Outcome Rate at Test Of Cure (TOC) Visit

End point title	Number of Participants With Favorable Per-pathogen Microbiological Outcome Rate at Test Of Cure (TOC) Visit
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End point description:

A total of 24 pathogens in the doripenem group and 6 pathogens in the meropenem group were isolated at baseline from the intra-abdominal culture and were susceptible to the study drug received. The most common pathogens isolated from the intra-abdominal culture are listed in the table below; the numbers in parenthesis next to each pathogen represent the number of participants with the pathogen isolated at baseline in the doripenem and meropenem treatment groups, respectively. The favourable per-pathogen microbiological outcome was considered when all baseline pathogens were eradicated (absence) or presumed eradicated (absence of material to culture in a participant who has a positive clinical response to treatment).

End point type	Secondary
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End point timeframe:

TOC (7 to 14 days after the last dose of study medication therapy)

End point values	Doripenem	Meropenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23 ^[17]	8 ^[18]		
Units: Participants				
number (not applicable)				
Streptococcus anginosus (n=13, 0)	9	0		
Escherichia coli (n=19, 8)	15	5		
Bacteroides fragilis (n=11, 1)	9	1		

Notes:

[17] - Microbiological intent-to-treat

[18] - Microbiological intent-to-treat

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Favorable Per-pathogen Microbiological Outcome Rate at Late Follow-Up (LFU) Visit

End point title	Number of Participants With Favorable Per-pathogen Microbiological Outcome Rate at Late Follow-Up (LFU) Visit
End point description:	
A total of 24 pathogens in the doripenem group and 6 pathogens in the meropenem group were isolated at baseline from the intra-abdominal culture and were susceptible to the study drug received. The most common pathogens isolated at baseline from the intra-abdominal culture are listed in the table below; the numbers in parenthesis next to each pathogen represent the number of participants with the pathogen isolated in the doripenem and meropenem treatment groups, respectively. The favourable per-pathogen microbiological outcome was considered when all baseline pathogens were eradicated (absence) or presumed eradicated (absence of material to culture in a participant who has a positive clinical response to treatment).	
End point type	Secondary
End point timeframe:	
LFU (28 to 42 days after the last dose of study medication therapy)	

End point values	Doripenem	Meropenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23 ^[19]	8 ^[20]		
Units: Participants				
number (not applicable)				
Streptococcus anginosus (n=13, 0)	9	0		
Escherichia coli (n=19, 8)	15	5		
Bacteroides fragilis (n=11, 1)	9	1		

Notes:

[19] - Microbiological intent-to-treat

[20] - Microbiological intent-to-treat

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Doripenem
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Reporting group description:

Doripenem 20 milligram per kilogram [mg/kg] per dose (up to 500 milligram per dose [mg/dose]) was administered every 8 hours as 60-minutes intravenous [IV] (at least 3 days of IV doripenem only or IV doripenem followed by oral amoxicillin/clavulanate potassium). Total duration of treatment 10 to 14 days.

Reporting group title	Meropenem
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Reporting group description:

Meropenem 20 milligram per kilogram [mg/kg] per dose (up to 1 gram per dose [g/dose]) was administered every 8 hours as 30-minutes intravenous [IV] (at least 3 days of IV meropenem only or IV meropenem followed by oral amoxicillin/clavulanate potassium). Total duration of treatment 10 to 14 days.

Serious adverse events	Doripenem	Meropenem	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 31 (22.58%)	0 / 10 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Seroma			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal Pain			

subjects affected / exposed	3 / 31 (9.68%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional Gastrointestinal Disorder			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (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: 3 %

Non-serious adverse events	Doripenem	Meropenem	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 31 (67.74%)	6 / 10 (60.00%)	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 10 (0.00%)	
occurrences (all)	2	0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood Chloride Increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram QT Prolonged			
subjects affected / exposed	0 / 31 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

Hepatic Enzyme Increased subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Gamma-Glutamyltransferase Increased subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	0 / 10 (0.00%) 0	
Injury, poisoning and procedural complications Procedural Site Reaction subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Seroma subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Vascular disorders Phlebitis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Cardiac disorders Ventricular Extrasystoles subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 10 (10.00%) 1	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Blood and lymphatic system disorders Eosinophilia subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	0 / 10 (0.00%) 0	
General disorders and administration site conditions Catheter Site Inflammation subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Infusion Site Pain subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	

Malaise subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Gastrointestinal disorders			
Abdominal Distension subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	1 / 10 (10.00%) 1	
Abdominal Pain subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 4	0 / 10 (0.00%) 0	
Abdominal Tenderness subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 3	0 / 10 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	2 / 10 (20.00%) 2	
Gastrointestinal Hypomotility subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Ileus subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 10 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	0 / 10 (0.00%) 0	
Tongue Ulceration subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 10 (10.00%) 1	
Vomiting subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	2 / 10 (20.00%) 2	
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 31 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Rash Papular			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences (all)	4	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Abscess			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Otitis Media			
subjects affected / exposed	0 / 31 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Peritonitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypervolaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2011	The overall reason for the amendment were: incorporate comments from regulatory authorities and investigators from around the world. There was change in meropenem time of intravenous bolus infusion from a 3 to 5 minute, to clarify directions and update the dosing of amoxicillin/clavulanate potassium to every 12 hours [q12h] (7:1 amoxicillin/clavulanate ratio), to allow subjects with negative intra-abdominal culture results to continue on study drug. Also to specify that subjects with recurrence of an intra-abdominal infection or who have failed prior surgical and/or medical therapy for a recent or ongoing infection may not enrol in the study. The amendment also includes the requirement that urinalysis with microscopy and creatinine clearance be calculated at baseline as well as to specify time points for the collection of safety laboratory tests. It also includes to align the protocol with the EU pediatric investigational plan (PIP) and to remove details of the IDMC that will be specified in the IDMC charter. The amended protocol includes to revise the pharmacokinetic sample collection and handling methods.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 June 2013	This study was terminated early due to business reasons and not related to safety concerns or issues. NOTE: Interruption date indicates the date on which IDMC was notified of premature termination of trial.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The major limitation of the study was limited enrollment which precludes a meaningful conclusion about the efficacy and safety of doripenem compared with meropenem.

Notes: