Clinical trial results:
A randomized, double-blind, multicenter trial to evaluate the safety and efficacy of sequential (intravenous, oral) moxifloxacin versus comparator in pediatric subjects with complicated intra-abdominal infection

Summary

EudraCT number	2009-015578-37
Trial protocol	DE ES LV LT CZ BE HU BG GR Outside EU/EEA
Global end of trial date	21 January 2015

Results information

Result version number	v1
This version publication date	12 July 2016
First version publication date	22 July 2015

Trial information

Trial identification

Sponsor protocol code	BAY12-8039/11643

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01069900
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer HealthCare AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com
Scientific contact	Therapeutic Area Head, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.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	21 January 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of treatment with moxifloxacin (compared to the safety of intravenous (IV) ertapenem followed by per oral (PO) amoxicillin/clavulanate).

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects and/or their legally authorized representative. Participating subjects and/or their legally authorized representative signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 July 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	15 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 69
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	Czech Republic: 9
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Lithuania: 25
Country: Number of subjects enrolled	Latvia: 88
Country: Number of subjects enrolled	Mexico: 27
Country: Number of subjects enrolled	Peru: 3
Country: Number of subjects enrolled	Romania: 26
Country: Number of subjects enrolled	Russian Federation: 10
Country: Number of subjects enrolled	Ukraine: 159
Country: Number of subjects enrolled	United States: 6

Worldwide total number of subjects	478
EEA total number of subjects	255

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)	1
Children (2-11 years)	177
Adolescents (12-17 years)	300
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at multicenter between 21 July 2010 (first subject first visit) to 21 January 2015 (last subject last visit).

Pre-assignment

Screening details:

Overall 478 subjects were enrolled, 20 subjects had screening failures hence, 458 subjects were randomized to receive treatment.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Moxifloxacin (Avelox, BAY12-8039)

Arm description:

Subjects randomized to the moxifloxacin arm of this study received intravenous moxifloxacin plus ertapenem placebo (0.9 % sodium chloride [NaCl solution]) for a minimum of 3 days and, if switched to oral treatment, PO moxifloxacin plus PO amoxicillin/clavulanate placebo. Total treatment duration is 5-14 days.

Arm type	Experimental
Investigational medicinal product name	Moxifloxacin
Investigational medicinal product code	BAY12-8039
Other name	
Pharmaceutical forms	Injection, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

For subjects 12 to less than (<) 18 years of age and weighing at least 45 kilograms (kg), the dose of moxifloxacin will be 400 milligrams (mg), once daily (OD). Subjects 12 to < 18 years of age and weighing less than 45 kg, the dose of moxifloxacin will be 4 mg/kg twice daily (BID), every 12 hours (q12h), not exceeding 400 mg/day. Subjects 6 to < 12 years of age the dose of moxifloxacin will be 4mg/kg, q12h, not exceeding 400 mg/day. Subjects 2 to less than 6 years of age the dose of moxifloxacin will be 5mg/kg, q12h, not exceeding 400 mg/day. Subjects 3 months to less than 2 years of age the dose of moxifloxacin will be 6mg/kg q12h IV, not exceeding 400 mg/day. Subjects who were switched from IV to PO therapy, 400 mg or 50 mg moxifloxacin tablets were provided.
Sterile 0.9% sodium chloride solution intended for IV use was used as the placebo for IV moxifloxacin. Tablets containing inactive ingredients were used as the placebo for PO moxifloxacin 400 mg and 50 mg tablets.

Arm title	Comparator Ertapenem

Arm description:

Subjects randomized to the comparator arm of this study received intravenous ertapenem plus moxifloxacin placebo (0.9 % NaCl solution) for a minimum of 3 days and, if switched to oral treatment, amoxicillin/clavulanate as an oral suspension plus PO moxifloxacin placebo. Total treatment duration is 5-14 days.

Arm type	Active comparator

Investigational medicinal product name	Ertapenem
Investigational medicinal product code	
Other name	Invaz
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

For subjects 13 to <18 years of age, the dosage of ertapenem were 1 gram (g) OD. For subjects 3 months to < 13 years of age, the dosage was 15 mg/kg q12h not to exceed 1 g/day.

Investigational medicinal product name	Clavulanate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension and solvent for suspension for injection
Routes of administration	Oral use

Dosage and administration details:

Subjects 2 years to < 18 years of age who were switched from IV to PO therapy receive clavulanate suspension. The dosage of clavulanate was 3.2 mg/kg q12h. (maximum dose of clavulanate was 125 mg q12h).

Investigational medicinal product name	Amoxicillin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension and solvent for suspension for injection
Routes of administration	Oral use

Dosage and administration details:

Subjects 2 years to < 18 years of age who were switched from IV to PO therapy receive amoxicillin suspension. The dosage of amoxicillin was 22.5 mg q12h (a maximum dose of 875 mg amoxicillin q12h must not be exceeded).

Number of subjects in period 1[1]	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem
Started	305	153
Treated	301	150
Completed	287	149
Not completed	18	4
Consent withdrawn by subject	6	1
Technical problems	-	1
Protocol Violation	4	1
Lost to follow-up	7	1
Insufficient Therapeutic effect	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline period included only the treated subjects. Due to screen failure, not all enrolled subjects were randomized and treated with study drugs.

Baseline characteristics

Reporting groups

Reporting group title	Moxifloxacin (Avelox, BAY12-8039)

Reporting group description:

Subjects randomized to the moxifloxacin arm of this study received intravenous moxifloxacin plus ertapenem placebo (0.9 % sodium chloride [NaCl solution]) for a minimum of 3 days and, if switched to oral treatment, PO moxifloxacin plus PO amoxicillin/clavulanate placebo. Total treatment duration is 5-14 days.

Reporting group title	Comparator Ertapenem

Reporting group description:

Subjects randomized to the comparator arm of this study received intravenous ertapenem plus moxifloxacin placebo (0.9 % NaCl solution) for a minimum of 3 days and, if switched to oral treatment, amoxicillin/clavulanate as an oral suspension plus PO moxifloxacin placebo. Total treatment duration is 5-14 days.

Reporting group values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem	Total
Number of subjects	305	153	458
Age categorical Units: Subjects			
12-<18 years	190	94	284
6-<12 years	100	52	152
2-<6 years	14	7	21
3 months - <2 years	1	0	1
Age continuous Units: years			
arithmetic mean	12.05	12.046	
standard deviation	± 3.66	± 3.495	-
Gender categorical Units: Subjects			
Female	124	53	177
Male	181	100	281

Subject analysis sets

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects (N= 451) treated with at least one dose of study medication.

Reporting group values	Safety analysis set		
Number of subjects	451		
Age categorical Units: Subjects			
12-<18 years	278		
6-<12 years	151		
2-<6 years	21		
3 months - <2 years	1		

Age continuous Units: years			
arithmetic mean	12.038		
standard deviation	± 3.61		
Gender categorical Units: Subjects			
Female	174		
Male	277		

End points

End points reporting groups

Reporting group title	Moxifloxacin (Avelox, BAY12-8039)

Reporting group description:

Subjects randomized to the moxifloxacin arm of this study received intravenous moxifloxacin plus ertapenem placebo (0.9 % sodium chloride [NaCl solution]) for a minimum of 3 days and, if switched to oral treatment, PO moxifloxacin plus PO amoxicillin/clavulanate placebo. Total treatment duration is 5-14 days.

Reporting group title	Comparator Ertapenem

Reporting group description:

Subjects randomized to the comparator arm of this study received intravenous ertapenem plus moxifloxacin placebo (0.9 % NaCl solution) for a minimum of 3 days and, if switched to oral treatment, amoxicillin/clavulanate as an oral suspension plus PO moxifloxacin placebo. Total treatment duration is 5-14 days.

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects (N= 451) treated with at least one dose of study medication.

Primary: Number of Subjects With Adverse Events

End point title	Number of Subjects With Adverse Events[1]

End point description:

An adverse event (AE) was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly.

End point type	Primary

End point timeframe:

All AEs and SAE were recorded from treatment start to test of cure visit; musculoskeletal AEs were recorded up to 1 year post-end of treatment (EOT) visit; subjects with musculoskeletal AEs 1 year after EOT were followed up to 5 years or until resolution.

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	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[2]	150[3]		
Units: Subjects				
Any AE	175	82		
Any SAE	20	6		

Notes:

[2] - Safety analysis set

[3] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinical Cardiac Adverse Events

End point title	Number of Subjects With Clinical Cardiac Adverse Events[4]

End point description:

End point type	Primary

End point timeframe:

All AEs and SAE were recorded from treatment start to test of cure visit; musculoskeletal AEs were recorded up to 1 year post-end of treatment (EOT) visit; subjects with musculoskeletal AEs 1 year after EOT were followed up to 5 years or until resolution.

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	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[5]	150[6]		
Units: Subjects				
Any AE	38	7		
Any SAE	0	0		

Notes:

[5] - Safety analysis set

[6] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Musculoskeletal Adverse Events

End point title	Number of Subjects With Musculoskeletal Adverse Events[7]

End point description:

End point type	Primary

End point timeframe:

All AEs and SAE were recorded from treatment start to test of cure visit; musculoskeletal AEs were recorded up to 1 year post-end of treatment (EOT) visit; subjects with musculoskeletal AEs 1 year after EOT were followed up to 5 years or until resolution.

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	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[8]	150[9]		
Units: Subjects				
Any AE	13	5		
Any SAE	1	0		

Notes:

[8] - Safety analysis set

[9] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence Rates of Musculoskeletal Adverse Events by Primary System Organ Class (SOC) and Preferred Term

End point title	Incidence Rates of Musculoskeletal Adverse Events by Primary System Organ Class (SOC) and Preferred Term

End point description:

Musculoskeletal adverse events were classified as following SOCs (preferred terms): "injury, poisoning and procedural complications" (forearm fracture, joint injury, ligament sprain, muscle strain) "musculoskeletal and connective tissue disorders" (arthralgia, joint swelling, musculoskeletal pain, myalgia). Incidence rates were reported as percentage of subjects categorized under preferred terms.

End point type	Secondary

End point timeframe:

All AEs and SAE were recorded from treatment start to test of cure visit; musculoskeletal AEs were recorded up to 1 year post-end of treatment (EOT) visit; subjects with musculoskeletal AEs 1 year after EOT were followed up to 5 years or until resolution.

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[10]	150[11]		
Units: Percentage of subjects				
number (confidence interval 95%)				
Forearm fracture	0.003 (0.0001 to 0.0184)	0 (0 to 0.0243)		
Joint injury	0 (0 to 0.0122)	0.007 (0.0002 to 0.0366)		
Ligament sprain	0.003 (0.0001 to 0.0184)	0.007 (0.0002 to 0.0366)		
Muscle strain	0 (0 to 0.0122)	0.007 (0.0002 to 0.0366)		
Arthralgia	0.03 (0.0138 to 0.056)	0.013 (0.0016 to 0.0473)		
Joint swelling	0 (0 to 0.0122)	0.007 (0.0002 to 0.0366)		
Musculoskeletal pain	0.01 (0.0021 to 0.0288)	0 (0 to 0.0243)		
Myalgia	0.003 (0.0001 to 0.0184)	0 (0 to 0.0243)		

Notes:

[10] - Safety analysis set

[11] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Heart Rate Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point title	Heart Rate Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point description:

"N" signifies subjects who were evaluable for the specified parameter for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[12]	150[13]		
Units: Beats per minute (bpm)				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (N= 300, 150)	93.4 (± 19.1)	90.4 (± 16.9)		
Change at Day 1 ((N= 294, 148)	2.8 (± 9.7)	0.3 (± 6.9)		
Day 3: Pre-dose (N= 293, 146)	84.3 (± 17.2)	82.6 (± 16.2)		
Change at Day 3 (N= 290, 146)	1 (± 8.9)	-0.9 (± 7.1)		

Notes:

[12] - Safety analysis set

[13] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: PR Interval Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point title	PR Interval Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point description:

The PR interval is defined as the period that extends from the onset of atrial depolarization (beginning of the P wave) until the onset of ventricular depolarization. "N" signifies subjects who were evaluable for the specified parameter for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[14]	150[15]		
Units: milliseconds				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (N= 299, 150)	136.8294 (± 18.3554)	140.5933 (± 20.5113)		
Change at Day 1 (N= 292, 148)	0.7123 (± 8.2587)	-0.0203 (± 8.5631)		
Day 3: Pre-dose (N= 293, 146)	139.4915 (± 17.3258)	139.5685 (± 20.8174)		
Change at Day 3 (N= 289, 146)	1.5813 (± 9.2143)	1.5616 (± 9.9322)		

Notes:

[14] - Safety analysis set

[15] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: RR Interval Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point title	RR Interval Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point description:

The RR interval refers to the respective time interval in the Electrocardiogram. "N" signifies subjects who were evaluable for the specified parameter for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[16]	150[17]		
Units: milliseconds				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (N= 300, 150)	670.7567 (± 142.6153)	689.3067 (± 145.5957)		
Change at Day 1 (N= 294, 148)	-20.6429 (± 74.3401)	-3.4797 (± 56.9955)		
Day 3: Pre-dose (N= 293, 146)	740.4778 (± 149.0964)	754.6027 (± 150.1203)		
Change at Day 3 (N= 290, 146)	-9.2862 (± 77.7582)	10.5137 (± 67.1124)		

Notes:

[16] - Safety analysis set

[17] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: QRS Interval Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point title	QRS Interval Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point description:

The QRS interval represents the time it takes for ventricular depolarization to occur. "N" signifies subjects who were evaluable for the specified parameter for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[18]	150[19]		
Units: milliseconds				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (N= 300, 150)	89.0333 (± 7.8279)	88.8067 (± 7.9264)		
Change at Day 1 (N= 294, 148)	0.119 (± 4.3799)	1.223 (± 4.2568)		
Day 3: Pre-dose (N= 293, 146)	89.2423 (± 8.0196)	89.3904 (± 7.8198)		
Change at Day 3 (N= 289, 146)	0.2768 (± 4.123)	0.2877 (± 3.1687)		

Notes:

[18] - Safety analysis set

[19] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: QT Interval Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point title	QT Interval Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point description:

The QT interval is the period that extends from the beginning of ventricular depolarization until the end

of ventricular repolarization. "N" signifies subjects who were evaluable for the specified parameter for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[20]	150[21]		
Units: milliseconds				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (N= 298, 150)	341.1812 (± 33.9858)	344.2333 (± 33.5494)		
Change at Day 1 (N= 290, 148)	2.5828 (± 15.213)	1.1149 (± 11.5744)		
Day 3: Pre-dose (N= 292, 146)	358.3082 (± 34.0504)	356.5822 (± 35.6653)		
Change at Day 3 (N= 287, 146)	6.0906 (± 16.1875)	3.1644 (± 11.9586)		

Notes:

[20] - Safety analysis set

[21] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Corrected QT (QTc) Interval Calculated (Calc) Bazett Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point title	Corrected QT (QTc) Interval Calculated (Calc) Bazett Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point description:

QTc interval Calc Bazett represent the interval corrected for heart rate (QTc) milliseconds (msec) which was calculated by Bazett’s method. "N" signifies subjects who were evaluable for the specified parameter for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[22]	150[23]		
Units: milliseconds				
arithmetic mean (standard deviation)				

Day 1: Pre-dose (N= 298, 150)	419.5872 (± 19.3278)	417.34 (± 18.5718)		
Change at Day 1 (N= 290, 148)	9.731 (± 14.2961)	2.2905 (± 14.2544)		
Day 3: Pre-dose (N= 292, 146)	419.2055 (± 16.6815)	412.7945 (± 17.0075)		
Change at Day 3 (N= 287, 146)	9.2509 (± 16.8132)	1 (± 12.5346)		

Notes:

[22] - Safety analysis set

[23] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Corrected QT (QTc) Interval Calculated (Calc) Fridericia Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point title	Corrected QT (QTc) Interval Calculated (Calc) Fridericia Changes in Electrocardiogram (ECG) Profiles From Pre-dose to Post-dose on Treatment Day 1 and Treatment Day 3

End point description:

QTc interval Calc Fridericia represent the interval corrected for heart rate (QTc) msec which was calculated by Fridericia's method. "N" signifies subjects who were evaluable for the specified parameter for each arm, respectively.

End point type	Secondary

End point timeframe:

Baseline (Pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[24]	150[25]		
Units: milliseconds				
arithmetic mean (standard deviation)				
Day 1: Pre-dose (N= 298, 150)	391.1846 (± 19.1574)	390.9467 (± 18.4339)		
Change at Day 1 (N= 290, 148)	7.0724 (± 11.3219)	1.9122 (± 11.3058)		
Day 3: Pre-dose (N= 292, 146)	397.3767 (± 17.2179)	392.6918 (± 18.8144)		
Change at Day 3 (N= 287, 146)	8.115 (± 13.5805)	1.774 (± 9.3328)		

Notes:

[24] - Safety analysis set

[25] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Potentially Clinically Significant Electrocardiogram (ECG) QTc Interval

Prolongation - by QTc Interval Calc Fridericia Correction on Treatment Day 1 and During Therapy Day 3

End point title	Potentially Clinically Significant Electrocardiogram (ECG) QTc Interval Prolongation - by QTc Interval Calc Fridericia Correction on Treatment Day 1 and During Therapy Day 3

End point description:

A significant QTc prolongation was considered when the QTc value was more than (>) upper limit of normal (ULN) range or was prolonged for 30 msec or 60msec in comparison with the pre-treatment value measured on Day 1. "N" signifies subjects who were evaluable for the specified parameter for each arm, respectively. Percentage of subjects with potentially clinically significant ECG data was reported.

End point type	Secondary

End point timeframe:

Baseline (pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[26]	150[27]		
Units: Percentage of subjects				
number (not applicable)				
Day1: Pre-dose QTcCalcFridericia>ULN (N= 300, 150)	0.7	1.3		
Day1: Post-dose QTcCalcFridericia>ULN (N= 297,148)	3	2		
Day1: Post-dose >30 ms from pre-dose (N= 297,148)	2	0		
Day1: Post-dose >60 ms from pre-dose (N= 297,148)	0.3	0		
Day3: Pre-dose QTcCalcFridericia>ULN (N= 293, 146)	1.4	1.4		
Day3: Post-dose QTcCalcFridericia>ULN (N= 291,148)	9.6	1.4		
Day3: Post-dose >30 ms from pre-dose (N= 291,148)	17.9	3.4		
Day3: Post-dose >60 ms from pre-dose (N= 291,148)	1.7	0.7		

Notes:

[26] - Safety analysis set

[27] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Potentially Clinically Significant Electrocardiogram (ECG) QTc Interval Prolongation - by QTc Calc Bazett Correction on Treatment Day 1 and During Therapy Day 3

End point title	Potentially Clinically Significant Electrocardiogram (ECG) QTc Interval Prolongation - by QTc Calc Bazett Correction on Treatment Day 1 and During Therapy Day 3

End point description:

A significant QTc prolongation was considered when the QTc value was more than ULN range or was prolonged for 30 msec or 60msec in comparison with the pre-treatment value measured on Day 1. "N"

signifies subjects who were evaluable for the specified parameter for each arm, respectively. Percentage of subjects with potentially clinically significant ECG data was reported.

End point type	Secondary

End point timeframe:

Baseline (pre-dose), Day 1, Day 3

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	301[28]	150[29]		
Units: Percentage of subjects				
number (not applicable)				
Day1: Pre-dose QTc Calc Bazett > ULN (N= 300, 150)	7.7	2.7		
Day1: Post-dose QTc Calc Bazett > ULN (N= 297,148)	16.2	4.1		
Day1: Post-dose >30 ms from pre-dose (N= 297,148)	5.4	0		
Day1: Post-dose >60 ms from pre-dose (N= 297,148)	0	0		
Day3: Pre-dose QTc Calc Bazett > ULN (N= 293, 146)	3.8	1.4		
Day3: Post-dose QTc Calc Bazett > ULN (N= 291,148)	15.5	3.4		
Day3: Post-dose >30 ms from pre-dose (N= 291,148)	9.6	2		
Day3: Post-dose >60 ms from pre-dose (N= 291,148)	0.7	0.7		

Notes:

[28] - Safety analysis set

[29] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response at Test-of-Cure (TOC) Visit

End point title	Clinical Response at Test-of-Cure (TOC) Visit

End point description:

Clinical responses were graded as clinical cure, failure or indeterminate. 'Clinical cure' defined as a resolution or sufficient improvement of clinical signs and symptoms related to the infection; 'failure' defined as a reappearance of the signs and symptoms of the original infection, or wound infection requiring further systemic antimicrobial therapy; 'indeterminate' defined as those subjects in whom a clinical assessment was not possible to determine (due to early withdrawal from the study because of adverse events, protocol violation, withdrawn consent). Percentage of subjects with clinical response at TOC were reported.

End point type	Secondary

End point timeframe:

28 to 42 days

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297[30]	150[31]		
Units: Percentage of subjects				
number (not applicable)				
Clinical Cure	86.2	95.3		
Clinical Failure	5.7	2		
Indeterminate	8.1	2.7		

Notes:

[30] - Safety analysis set with subjects evaluable for this outcome

[31] - Safety analysis set

Statistical analyses

No statistical analyses for this end point

Secondary: Bacteriological Response at Test-of-Cure (TOC) Visit

End point title	Bacteriological Response at Test-of-Cure (TOC) Visit

End point description:

Bacteriological responses were graded as presumed persistence, presumed eradication or indeterminate. 'Presumed persistence' was applicable for subjects judged to be clinical failures, and appropriate culture material is not available for evaluation; 'presumed eradication' defined as the absence of appropriate culture material for evaluation because the subject has clinically responded and invasive procedures are not warranted; índeterminate' was applicable when the bacteriological response to the study drug was not valid for any reason (eg, pre-treatment culture was negative or culture was not obtained when material was available and the subject was not judged a clinical failure). Percentage of subjects with bacteriological response at TOC were reported.

End point type	Secondary

End point timeframe:

28 to 42 days

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249[32]	136[33]		
Units: Percentage of subjects				
number (not applicable)				
Presumed Persistence	6.8	2.2		
Presumed Eradication	84.7	94.9		
Indeterminate	8.4	2.9		

Notes:

[32] - Safety analysis set with subjects evaluable for this outcome

[33] - Safety analysis set with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response at Test-of-Cure (TOC) Visit in Subjects With

Bacteriologically Confirmed Complicated Intra-abdominal Infection (cIAI)

End point title	Clinical Response at Test-of-Cure (TOC) Visit in Subjects With Bacteriologically Confirmed Complicated Intra-abdominal Infection (cIAI)

End point description:

Clinical responses were graded as clinical cure, failure or indeterminate. 'Clinical cure' defined as a resolution or sufficient improvement of clinical signs and symptoms related to the infection; 'failure' defined as a reappearance of the signs and symptoms of the original infection, or wound infection requiring further systemic antimicrobial therapy; 'indeterminate' defined as those subjects in whom a clinical assessment was not possible to determine (due to early withdrawal from the study because of adverse events, protocol violation, withdrawn consent). Percentage of subjects with clinical response at TOC were reported

End point type	Secondary

End point timeframe:

28 to 42 days

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297[34]	150[35]		
Units: Percentage of subjects				
number (not applicable)				
Clinical Cure	86.2	95.3		
Clinical Failure	5.7	2		
Indeterminate	8.1	2.7		

Notes:

[34] - Safety analysis set with subjects evaluable for this outcome

[35] - Safety analysis set with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response at a 'During Therapy' Visit

End point title	Clinical Response at a 'During Therapy' Visit

End point description:

Clinical responses during therapy visit were graded as clinical improvement, clinical failure, or indeterminate. Clinical improvement defined as a reduction in the severity and/or the number of signs and symptoms of infection; 'clinical failure' defined as a failure to respond or insufficient lessening of the signs and symptoms of infection requiring a modification or addition of antibacterial therapy. 'Indeterminate' defined as those subjects in whom a clinical assessment is not possible to determine (eg, due to early withdrawal from the study because of adverse events, protocol violation, withdrawn consent, receipt of an effective concomitant antibacterial for an indication other than the study indication and receipt of less than 3 full days of study drug, etc). Percentage of subjects with clinical response during therapy visit were reported.

End point type	Secondary

End point timeframe:

Day 3 to Day 5

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[36]	148[37]		
Units: Percentage of subjects				
number (not applicable)				
Clinical Improvement	94.3	98		
Clinical Failure	1	0.7		
Indeterminate	4.7	1.4		

Notes:

[36] - Safety analysis set with subjects evaluable for this outcome

[37] - Safety analysis set with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Secondary: Bacteriological Response at a 'During Therapy' Visit

End point title	Bacteriological Response at a 'During Therapy' Visit

End point description:

Bacteriological response during therapy were graded as presumed persistence, presumed eradication, or indeterminate'Presumed persistence' is applicable for subjects judged to be clinical failures and appropriate culture material is not available for evaluation;'presumed eradication' is defined as the absence of appropriate culture material for evaluation because the subject has clinically responded (with a response as a resolution or cure) and invasive procedures are not warranted; 'indeterminate is applicable when the bacteriological response to the study drug is not valid for any reason (eg, pre-treatment culture was negative or culture was not obtained when material was available and the subject is not judged a clinical failure). Percentage of subjects with bacteriological response during therapy visit were reported

End point type	Secondary

End point timeframe:

Day 3 to Day 5

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249[38]	134[39]		
Units: Percentage of subjects				
number (not applicable)				
Presumed Persistence	1.2	0.7		
Presumed Eradication	95.6	97.8		
Indeterminate	3.2	1.5		

Notes:

[38] - Safety analysis set with subjects evaluable for this outcome

[39] - Safety analysis set with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Response at the End-of-Treatment (EOT) Visit

End point title	Clinical Response at the End-of-Treatment (EOT) Visit

End point description:

Clinical responses at EOT were graded as resolution, failure, or indeterminate. 'Resolution' defined as a disappearance of signs and symptoms related to the infection or sufficient improvement of clinical signs and symptoms related to the infection and the subject does not require any further antibiotic therapy or surgical intervention; 'failure' defined as worsening or insufficient lessening of the signs and symptoms of infection requiring a modification or addition of antibacterial therapy; 'indeterminate' is defined as those subjects in whom a clinical assessment is not possible to determine (eg, due to early withdrawal from the study because of adverse events, protocol violation, withdrawn consent; receipt of less than 3 full days of study drug; receipt of an effective concomitant antibacterial for an indication other than study indication; etc). Percentage of subjects with clinical response at EOT were reported.

End point type	Secondary

End point timeframe:

Day 5 to Day 14

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283[40]	148[41]		
Units: Percentage of subjects				
number (not applicable)				
Resolution	92.2	98		
Clinical Failure	4.6	0.7		
Indeterminate	3.2	1.4		

Notes:

[40] - Safety analysis set with subjects evaluable for this outcome

[41] - Safety analysis set with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Secondary: Bacteriological response at the End of Treatment (EOT) visit

End point title	Bacteriological response at the End of Treatment (EOT) visit

End point description:

Bacteriological response at EOT were grades as presumed persistence, presumed eradication or indeterminate. 'presumed persistence' was applicable for subjects judged to be clinical failures and appropriate culture material is not available for evaluation; 'presumed eradication' defined as the absence of appropriate culture material for evaluation because the subject has clinically responded (with a response as a resolution or cure) and invasive procedures are not warranted; 'indeterminate' is applicable when the bacteriological response to the study drug was not valid for any reason (eg, pre-treatment culture was negative or culture was not obtained when material was available and the subject was not judged a clinical failure). Percentage of subjects with bacteriological response at EOT were reported.

End point type	Secondary

End point timeframe:

Day 5 to Day 14

End point values	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237[42]	134[43]		
Units: Percentage of subjects				
number (not applicable)				
Presumed Persistence	5.5	0.7		
Presumed Eradication	91.1	97.8		
Indeterminate	3.4	1.5		

Notes:

[42] - Safety analysis set with subjects evaluable for this outcome

[43] - Safety analysis set with subjects evaluable for this outcome

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs and SAE were recorded from treatment start to test of cure visit; musculoskeletal AEs were recorded up to 1 year post-end of treatment (EOT) visit; subjects with musculoskeletal AEs 1 year after EOT were followed up to 5 years or until resolution.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Moxifloxacin (Avelox, BAY12-8039)

Reporting group description:

Subjects randomized to the moxifloxacin arm of this study received intravenous moxifloxacin plus ertapenem placebo (0.9 % NaCl solution) for a minimum of 3 days and, if switched to oral treatment, PO moxifloxacin plus PO amoxicillin/clavulanate placebo. Total treatment duration is 5-14 days.

Reporting group title	Comparator Ertapenem

Reporting group description:

Subjects randomized to the comparator arm of this study received intravenous ertapenem plus moxifloxacin placebo (0.9 % NaCl solution) for a minimum of 3 days and, if switched to oral treatment, amoxicillin/clavulanate as an oral suspension plus PO moxifloxacin placebo. Total treatment duration is 5-14 days.

Serious adverse events	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem	
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 301 (6.64%)	6 / 150 (4.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 301 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wound dehiscence			

subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Phimosis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 301 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic generalised epilepsy			
subjects affected / exposed	0 / 301 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Surgical failure			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			

subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal perforation			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 301 (0.66%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	3 / 301 (1.00%)	2 / 150 (1.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocutaneous fistula			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecalith			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional gastrointestinal disorder			
subjects affected / exposed	2 / 301 (0.66%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fasciitis			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (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 wall abscess			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 301 (0.00%)	1 / 150 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal abscess			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed	3 / 301 (1.00%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 301 (0.33%)	0 / 150 (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: 1 %

Non-serious adverse events	Moxifloxacin (Avelox, BAY12-8039)	Comparator Ertapenem	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	127 / 301 (42.19%)	63 / 150 (42.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 301 (1.00%)	2 / 150 (1.33%)	
occurrences (all)	3	2	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 301 (0.66%)	3 / 150 (2.00%)	
occurrences (all)	2	3	
Blood creatine phosphokinase increased			
subjects affected / exposed	4 / 301 (1.33%)	2 / 150 (1.33%)	
occurrences (all)	4	2	
Electrocardiogram QT prolonged			
subjects affected / exposed	28 / 301 (9.30%)	4 / 150 (2.67%)	
occurrences (all)	31	4	
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 301 (0.66%)	2 / 150 (1.33%)	
occurrences (all)	2	2	
Lipase increased			
subjects affected / exposed	1 / 301 (0.33%)	2 / 150 (1.33%)	
occurrences (all)	1	2	
Injury, poisoning and procedural complications			
Wound complication			
subjects affected / exposed	4 / 301 (1.33%)	2 / 150 (1.33%)	
occurrences (all)	4	2	
Incision site pain			
subjects affected / exposed	26 / 301 (8.64%)	14 / 150 (9.33%)	
occurrences (all)	26	14	
Postoperative wound complication			
subjects affected / exposed	3 / 301 (1.00%)	2 / 150 (1.33%)	
occurrences (all)	4	2	
Procedural pain			

subjects affected / exposed	16 / 301 (5.32%)	10 / 150 (6.67%)	
occurrences (all)	16	10	
Incision site inflammation			
subjects affected / exposed	2 / 301 (0.66%)	3 / 150 (2.00%)	
occurrences (all)	2	3	
Procedural vomiting			
subjects affected / exposed	0 / 301 (0.00%)	4 / 150 (2.67%)	
occurrences (all)	0	4	
Vascular disorders			
Phlebitis			
subjects affected / exposed	8 / 301 (2.66%)	0 / 150 (0.00%)	
occurrences (all)	8	0	
Surgical and medical procedures			
Abdominal cavity drainage			
subjects affected / exposed	0 / 301 (0.00%)	2 / 150 (1.33%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 301 (1.99%)	2 / 150 (1.33%)	
occurrences (all)	6	2	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 301 (1.99%)	4 / 150 (2.67%)	
occurrences (all)	6	4	
Infusion site phlebitis			
subjects affected / exposed	4 / 301 (1.33%)	0 / 150 (0.00%)	
occurrences (all)	6	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 301 (2.66%)	3 / 150 (2.00%)	
occurrences (all)	8	3	
Diarrhoea			
subjects affected / exposed	11 / 301 (3.65%)	1 / 150 (0.67%)	
occurrences (all)	12	1	
Nausea			

subjects affected / exposed	1 / 301 (0.33%)	2 / 150 (1.33%)	
occurrences (all)	1	2	
Vomiting			
subjects affected / exposed	20 / 301 (6.64%)	12 / 150 (8.00%)	
occurrences (all)	22	12	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 301 (2.99%)	2 / 150 (1.33%)	
occurrences (all)	36	2	
Joint swelling			
subjects affected / exposed	0 / 301 (0.00%)	2 / 150 (1.33%)	
occurrences (all)	0	2	
Infections and infestations			
Wound infection			
subjects affected / exposed	13 / 301 (4.32%)	6 / 150 (4.00%)	
occurrences (all)	13	6	
Metabolism and nutrition disorders			
Hyperlipasaemia			
subjects affected / exposed	1 / 301 (0.33%)	2 / 150 (1.33%)	
occurrences (all)	1	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2010	1. The sample size was increased from 300 to 450 patients. 2. Stratification of subjects by age was added to the protocol which allows a statistical analysis by age group. 3. A yearly follow-up up to 5 years after EOT was added if a musculoskeletal event has not resolved by the 1-Year Follow-up visit. This extended follow-up should ensure that subjects with unresolved musculoskeletal AEs are followed until resolution of the AE. 4. The list of drugs that might induce QTc prolongation and are therefore not allowed to be co-administered with moxifloxacin was expanded. 5. ECG measurement and interpretation of the results are explained in more detail. 6. Several additional examples of musculoskeletal related adverse events suggested by the FDA were added to the protocol. 7. The consistency of the descriptions of the musculoskeletal clinical and questionnaire assessments at different time points was improved. 8. Text describing how AEs which occur within 7 days of the EOT visit will be assessed and documented was added to the protocol.
30 August 2011	1. Inclusion and exclusion criteria changed. 2. Post-study therapy description amended. 3. Schedule of procedures amended to clarify procedures during Pre-treatment and During therapy periods of the study. 4. Various editorial changes, minor error correction and clarification were included in amendment 3, as well as revising the format for displaying the literature references.
07 August 2012	1. Clarifications with regards to ECG recordings as well as use of prior and concomitant medication that may influence QT interval have been added. 2. Clarification on when a premature termination visit is required has been added. 3. The possibility to contact patients by phone in case the do not return for follow-up visits has been introduced. 4. Various editorial changes, minor error correction and clarification were included in amendment 4.
29 January 2013	1. Clarifications were made regarding dosing for children 3 months to less than 2 years of age.
29 January 2013	1. Temporal artery was added as a method of body temperature measurement in addition to oral, rectal, and tympanic as this is commonly used in some countries. 2. The reporting period for adverse events (AEs, SAEs, including "Hy's Law" cases, and deaths) was changed from 7 days following EOT to the TOC visit as agreed to with the European Medicines Agency in the pediatric investigational plan. 3. The definition of significant renal impairment was modified to be consistent with the definition used in IV ertapenem comparator studies. 4. Quinolones have been excluded from allowed pre- and perioperative antibiotic treatment within 12 months prior to study entry. 5. Examination of the Achilles and patellar tendons was added to the skilled musculoskeletal assessment as recommended by an external expert. 6. Specific time points for the measurement of vital signs were added as recommended by the FDA. 7. The wording of the skilled musculoskeletal assessment questionnaire procedure was modified to refer to the correct visit. 8. Documentation of treatment of musculoskeletal AEs was added to be consistent with the CRF.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported