Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Bayer HealthCare

Clinical Trial Results Synopsis

Study Design Description		
Study Sponsor:	Bayer HealthCare AG	
Study Number:	11976	NCT00492726
Study Phase:	IIIb	
Official Study Title:	A prospective, randomized, double-dummy, double-blind, multicenter trial comparing the safety and efficacy of intravenous (IV) moxifloxacin 400 mg IV QD 24 hours to that of ertapenem 1.0 g IV QD 24 hours for 5 to 14 days for the treatment of subjects with complicated intra-abdominal infections (PROMISE study)	
Therapeutic Area:	Anti-Infectives	
Test Product		
Name of Test Product:	Moxifloxacin (Avelox, BAY12-8039)	
Name of Active Ingredient:	Moxifloxacin Hydrochloride	
Dose and Mode of Administration:	400 mg QD, IV	
Reference Therapy/Placebo		
Reference Therapy:	Ertapenem	
Dose and Mode of Administration:	1.0 g QD, IV	
Duration of Treatment:	Subjects were treated for a minimum of 5 days and a maximum of 14 days.	
Studied period:	**Date of first subjects' first visit:**	02 JUL 2006
	Date of last subjects' last visit:	05 FEB 2009
Premature Study Suspension / Termination:	No	
Substantial Study Protocol Amendments:	Amendment No.1 (dated 07 JUL 2006) specified the following changes (applicable to Germany): • Exclusion criterion 1was amended to identify methods of contraception that were considered reliable • Specifically defined the population with a clinically relevant heart failure with reduced left-ventricular ejection fraction that should not be enrolled • Included a list of all interactions (drug interactions, charcoal and food interactions), which were previously documented in the investigator brochure (IB) Amendment No. 2 (dated 16 OCT 2006) specified the instructions concerning the sequence of administration of study medication and sample handling in case the subject was temporarily not able to provide a written consent.	

	Amendment No. 3 (dated 04 SEP 2007) (applicable to Argentina) specified the exclusion of appendix as a source of complicated intra-abdominal infection (cIAI) from the sites of infections. Amendment No. 4 (dated 19 NOV 2007) (applicable to all countries) specified the definition of septic shock by the requirement of vasopressors for more than 4 consecutive hours to explicitly state that low doses of vasopressors were permitted as long as the subject was hemodynamically stable. Furthermore, the duration of administration of moderately high or high doses of vasopressors was extended from 4 to 12 hours. In addition, the antibiotic panel for susceptibility testing was modified and the extended spectrum beta-lactamase (ESBL) test for all *Enterobacteriaceae* species was added. Amendment No. 5 (dated 16 JAN 2008) (applicable to Eastern European countries) specified the exclusion of appendix as a source of cIAI from the sites of infections studied in centers located in Estonia, Latvia, Lithuania, Bulgaria and Romania.
Study Centre(s):	This study was conducted in 52 study centers in 14 countries: Argentina (9), Belgium (3), Bulgaria (4), Estonia (3), France (2), Germany (5), Greece (1), Israel (2), Latvia (6), Lithuania (4), Romania (5), Russia (3), South Africa (3), and Spain (2).
Methodology:	The study consisted of a pre-treatment period (assessment within 24 hours before initiation of study treatment), a during treatment period (daily during treatment with a complete assessment on treatment Day 5 ±1), an end of treatment (EOT) visit (assessment from treatment Day 5 to 14), and a test of cure (TOC) visit (assessment 21 to 28 days after EOT). If treatment duration was ≤6 days, during treatment assessment was not necessary. Subjects assessed as failures at EOT were to attend a visit 21 to 28 days after the last administration of alternative therapy. Subjects randomized to the moxifloxacin group were first administered placebo matching the comparator (ertapenem dummy) IV for 30 min immediately followed by moxifloxacin IV for 60 min. Subjects in the ertapenem group were first administered ertapenem IV for 30 min immediately followed by placebo matching moxifloxacin (moxifloxacin dummy) for 60 min. The total treatment duration was at the investigator's discretion (minimum 5 days to maximum 14 days) irrespective to which treatment group the subject was randomized. Efficacy was determined by clinical and bacteriological evaluations performed at pre-treatment, during treatment, at EOT, and at TOC or at the end of alternative antimicrobial therapy for subjects who failed study drug therapy. The safety of the treatment was monitored by physical examination findings, vital signs, laboratory assessments (hematology, clinical chemistry, urinalysis), concomitant medications, and by the reporting of adverse events (AEs).
Indication/ Main Inclusion Criteria:	Indication Complicated intra-abdominal infections (cIAI) Main Inclusion Criteria • Men or women ≥ 18 years of age. • Hospitalization.

	• Expected duration of treatment with IV antibiotics anticipated to be greater than equal to 5 full days but not exceeding 14 days. • Confirmed or suspected IAI defined as follows: For a confirmed IAI, a surgical procedure (laparotomy or laparoscopy) must have been performed within 24 hours prior to enrollment and should have revealed at least one of the following: • Gross peritoneal inflammation with purulent exudates (ie, peritonitis). • Intra-abdominal abscess. • Macroscopic intestinal perforation with localized or diffuse peritonitis. Subjects enrolled on the basis of a suspected intra-abdominal infection having: • Radiological evidence (abdominal plain films, computed tomography [CT], magnetic resonance imaging [MRI] or ultrasound) of gastrointestinal perforation or intra-abdominal abscess • The following signs and symptoms: ▪ At least one symptom referable to the abdominal cavity (e.g., nausea, vomiting, distension or pain), lasting for at least 24 h. ▪ At least one of the following signs: tenderness (with or without rebound), absent or diminished bowel sounds, abdominal wall rigidity. ▪ At least two of the following systemic inflammatory response syndrome criteria: ➢ Temperature > 38.3°C rectal or tympanic membrane, or temperature > 37.8°C oral or > 37.3°C axillary. ➢ Heart rate > 90/min. ➢ Respiratory rate > 20/min. ➢ White blood cells (WBC) > 12,000 cells/mm^3 or < 4,000 cells/mm^3. • The subject must have been scheduled for a surgical procedure (laparotomy or laparoscopy) within 24 h of enrollment in the study.
Study Objectives:	**Overall:** The objective of this study was to compare the safety and efficacy of IV moxifloxacin 400 mg administered once daily (QD) with that of IV ertapenem 1 g QD in adult subjects with a cIAI who required surgery and parenteral antibiotic therapy: • Moxifloxacin, 400 mg IV QD for 5 to 14 days • Ertapenem, 1.0 g IV QD for 5 to 14 days **Primary:** To demonstrate the non-inferiority of IV moxifloxacin 400 mg administered once daily (QD) with that of IV ertapenem 1 g QD in adult subjects with a cIAI who required surgery and parenteral antibiotic therapy.
Evaluation Criteria:	**Efficacy (Primary):** The primary efficacy variable was the clinical response assessed at 21 to 28 days after EOT (TOC visit).

	Efficacy (Secondary): Secondary efficacy variables were: • Clinical and bacteriological response on treatment Day 5 +/- 1 • Clinical and bacteriological response at EOT (Day 5 to 14) • Bacteriological response at the TOC visit (21 to 28 days after EOT) • Clinical response at the TOC visit in subjects with a bacteriologically documented cIAI • Mortality attributable to intra abdominal infections at the time of the TOC visit (21 to 28 days after EOT) • Duration of hospitalization (days) • Duration of hospitalization postoperatively (days) **Safety:** Safety evaluations were based on physical examinations (including that of the abdomen), AEs (non-serious AEs occurring after the first application of study medication up to 7 days after EOT, serious adverse events [SAEs] up to 21 days after EOT for subjects without alternative therapy), vital signs and laboratory results.
Statistical Methods:	All efficacy analyses and tabulation of efficacy data were performed for the per protocol (PP) population (primary efficacy population) as well as for the intent to treat (ITT) population (secondary efficacy population). In addition, analyses were performed on the ITT and PP with causative organism(s) (ITT/microbiologically evaluable [MBE] and PP/MBE populations, respectively) comprising those ITT or PP subjects in whom at least one causative organism was identified from an appropriate pretherapy culture. **Efficacy (Primary):** The primary efficacy analysis was performed on the PP population. Treatment groups (moxifloxacin versus comparator) were compared using the Cochran Mantel Haenszel (CMH) point estimate and 95% confidence interval (CI) for calculating the difference in clinical success rates, at TOC (21 to 28 days after EOT, where EOT was Day 5 to 14 days after start of treatment). For moxifloxacin to be considered not less effective than the comparator, the lower limit of the 95% CI (moxifloxacin - comparator) had to be greater than -0.10 (-10%). The DerSimonian and Laird test (Cochran's Q-Test) was used to test the homogeneity of differences across centers/cluster of centers. **Efficacy (Secondary):** As secondary efficacy analyses, clinical response as assessed by the investigator at the EOT and TOC visits, bacteriological response at the EOT and TOC visits, as well as clinical response at TOC visit in subjects with bacteriologically documented cIAI were analyzed in the same way as the primary efficacy variable. Other secondary variables, as well as efficacy results in subgroups, were analyzed descriptively.

	Safety: Safety parameters were analyzed descriptively.
Number of Subjects:	Of the 830 subjects enrolled at 52 active centers, 26 subjects were not randomized (17 subjects had a protocol violation, 2 subjects due to technical problems, 1 subject died before randomization, 2 subjects withdrew consent (one of them only documented later), 1 subject was not randomized according to an investigator decision, 1 subject switched to a commercial drug, and 2 subjects were not randomized due to "protocol driven decision point"). Of the 804 randomized subjects, 410 subjects were included in the moxifloxacin group and 394 subjects in the ertapenem group. Six subjects were excluded from the Safety/ITT population because they were not treated with study drug (3 subjects withdrew consent and 3 others had a violation of an inclusion/exclusion criterion). In total, 798 subjects were treated: 408 subjects in the moxifloxacin group (64 receiving first moxifloxacin IV and 344 receiving first placebo matching ertapenem) and 390 subjects in the ertapenem group (322 receiving first ertapenem IV and 68 first placebo matching moxifloxacin). Subjects included in each analysis population is summarized in Table 1. **Table 1: Subjects included in each analysis population**

	Moxifloxacin		Ertapenem	
	n	(%)	N	(%)
All subjects randomized	410	(100)	394	(100)
Valid for the Safety/ Intent to treat (ITT) population	408	(100)	390	(99)
Valid for Per Protocol (PP) population	352	(86)	347	(88)
Valid for ITT with causative organism(s) population (ITT/MBE)	340	(83)	308	(78)
Valid for PP with causative organism(s) population (PP/MBE)	297	(72)	276	(70)

Study Results

Results Summary — Subject Disposition and Baseline

Of the 804 randomized subjects, 764 subjects completed treatment (40 subjects were withdrawn between randomization and EOT visits) and 718 subjects completed the study, including follow-up (46 subjects were lost to follow-up). The number of randomized subjects by geographical region was as follows: Baltic countries, 259 (32.2%); Eastern Europe, 188 (23.4%); Western Europe, 132 (16.4%); South America, 127 (15.8%) and South Africa, 98 (12.2%).

In the per protocol (PP) population, a total of 449 (64%) subjects were men (moxifloxacin 218 [62%]; ertapenem 231 [67%]) and 250 (36%) subjects were women (moxifloxacin 134 [38%]; ertapenem 116 [33%]).

The mean age of subjects was 46.4 years (range; 18 to 93 years) (moxifloxacin 46.7 [18 to 88] years; ertapenem 46.1 [18 to 93] years).

The mean acute physiology and chronic health evaluation (APACHE) II score was 6.9 in the moxifloxacin group and 6.8 in the ertapenem group.

The most common cIAI diagnosis types were diffuse peritonitis (two or more quadrants),

localized peritonitis (limited to one quadrant) and single intra-abdominal abscess. The most common causes of infection were acute appendicitis and ulcer. The most common sites of infection were appendix, stomach, and duodenum. All PP subjects underwent surgery before the start of study treatment except 3 subjects in the moxifloxacin group and 4 subjects in the ertapenem group who received their first dose of study drug before surgery. For one subject in the moxifloxacin group, it was unknown whether first dose of study drug was given prior to or after surgery.

Analysis of each population by site, cause and type of infection and geographical region revealed no major differences between treatment groups. Demographics and baseline characteristics of infection were generally similar in both treatment groups in the PP and ITT populations, with the exception of C-reactive protein (CRP) value, which was significantly higher in the moxifloxacin group in the ITT population (p=0.012).

Results Summary — Efficacy

Clinical Response

Table 2 presents an overview of the efficacy results for clinical response at the TOC visit in the PP and ITT populations.

Table 2: Summary of clinical response rates at TOC (PP and ITT populations)

PP population	Moxifloxacin N=352	Ertapenem N=347	95% CI
Clinical Response	n (%)	n (%)	
Clinical cure	315 (89.5)	324 (93.4)	-7.9 to 0.4
Clinical failure	37 (10.5)	23 (6.6)	
Relapse	14 (4.0)	6 (1.7)	
Failure from EOT[a]	23 (6.5)	17 (4.9)	
ITT population	Moxifloxacin N=408	Ertapenem N=390	95% CI
Clinical Response	n (%)	n (%)	
Clinical cure	334 (81.9)	339 (86.9)	-9.9 to 0.0
Clinical failure	74 (18.1)	51 (13.1)	
Relapse	14 (3.4)	6 (1.5)	
Failure from EOT[a]	26 (6.4)	18 (4.6)	
Indeterminate	25 (6.1)	20 (5.1)	
Missing	9 (2.2)	7 (1.8)	

[a] Failures from EOT carried forward at TOC

The primary efficacy variable, success rate for clinical response at the TOC visit in the PP population, was similar in both treatment groups and the statistical hypothesis of inferiority of moxifloxacin to the comparator regimen could be rejected at the 2.5% level. A slightly greater number of subjects in the moxifloxacin group (n=24, 6.8%) than in the ertapenem group (n=9, 2.6%) developed a post-operative wound infection requiring alternative systemic antibiotic therapy, and therefore, were assessed as clinical failures. Excluding these wound infections, the clinical cure rates were 96.0% (315/328) and 95.9% (324/338) in the moxifloxacin and ertapenem groups, respectively.

Non-inferiority was also supported by the clinical efficacy results in the ITT population (Table 2), in the PP/MBE population (moxifloxacin 89.2%, ertapenem 92.0%, 95% CI [-7.6 to 1.9]) and ITT/MBE population (moxifloxacin 82.4%, ertapenem 85.4%, 95% CI [-8.8 to 2.2]) since the lower limit of the 95% CI for all these populations was greater than -10%.

Clinical success rates at the TOC visit in the PP and ITT populations are displayed by site,

type and cause of infection in Table 3.

Table 3: Clinical success rates at the TOC visit by primary site, cause and type of infection (PP and ITT populations)

	Moxifloxacin n/N (%)	Ertapenem n/N (%)
PP Population		
Site of infection		
Gall bladder	35/35 (100.0)	31/32 (96.9)
Appendix	157/175 (89.7)	174/182 (95.6)
Large bowel	40/50 (80)	31/39 (79.5)
Small bowel	18/22 (81.8)	20/24 (83.3)
Stomach or duodenum	61/63 (96.8)	61/62 (98.4)
Other	4/7 (57.1)	7/8 (87.5)
Cause of infection		
Cholecystitis	33/33 (100.0)	31/32 (96.9)
Diverticulitis	28/29 (96.6)	15/16 (93.8)
Trauma	16/19 (84.2)	21/23 (91.3)
Tumor	8/13 (61.5)	11/13 (84.6)
Previous surgery	9/15 (60.0)	6/9 (66.7)
Acute appendicitis	155/172 (90.1)	167/176 (94.9)
Ulcer	51/53 (96.2)	54/55 (98.2)
Other	15/18 (83.3)	19/23 (82.6)
Type of infection		
Single abscess	59/69 (85.5)	59/64 (92.2)
Multiple abscess	1/2 (50.0)	1/2 (50.0)
Peritonitis localized (limited to one quadrant)	93/100 (93)	90/96 (93.8)
Peritonitis diffuse (two or more quadrants)	162/181 (89.5)	174/185 (94.1)
ITT Population		
Site of infection		
Gall bladder	36/39 (92.3)	33/37 (89.2)
Appendix	160/186 (86.0)	181/197 (91.9)
Large bowel	45/59 (76.3)	32/50 (64.0)
Small bowel	21/32 (65.6)	22/28 (78.6)
Stomach or duodenum	65/81 (80.2)	64/69 (92.8)
Other	7/11 (63.6)	7/9 (77.8)
Cause of infection		
Cholecystitis	33/37 (89.2)	33/38 (86.8)
Diverticulitis	31/34 (91.2)	15/21 (71.4)
Trauma	19/28 (67.9)	24/28 (85.7)
Tumor	11/16 (68.8)	11/16 (68.8)
Previous surgery	10/19 (52.6)	7/11 (63.6)
Acute appendicitis	157/182 (86.3)	173/190 (91.1)
Ulcer	54/67 (80.6)	56/61 (91.8)
Other	19/25 (76.0)	20/25 (80.0)
Type of infection		
Single abscess	64/78 (82.1)	61/71 (85.9)
Multiple abscess	1/3 (33.3)	1/3 (33.3)
Peritonitis localized (limited to one quadrant)	98/115 (85.2)	97/112 (86.6)
Peritonitis diffuse (two or more quadrants)	171/212 (80.7)	180/203 (88.7)

In the PP population, the cure rate was numerically higher (but statistically not significant) in the ertapenem group than in the moxifloxacin group in subjects with an acute appendicitis (90.1% [155/172] moxifloxacin versus 94.9% [167/176] ertapenem). For the other frequent causes of infection (i.e., perforated ulcer, cholecystitis and diverticulitis), the response rates were similar in the two treatment groups. When analyzed by type of infection, the response rates were numerically higher (but statistically not significant) in the ertapenem group (92.2% and 94.1%) than in the moxifloxacin group (85.5% and 89.5%) for subjects with a

single abscess or diffuse peritonitis, respectively. In subjects with localized peritonitis, the cure rate was similar in moxifloxacin (93.0%) and ertapenem (93.8%) treated subjects.

Clinical improvement at the during therapy visit was seen in a similar number of PP subjects in each group: 210/352 (59.7%) in the moxifloxacin group and 194/347 (55.9%) in the ertapenem group, 95% CI: -0.4 to 2.7. The clinical response at the during therapy visit was not documented in 142 and 151 subjects of the moxifloxacin and ertapenem groups, respectively, since treatment duration was ≤6 days for these subjects who only had the EOT visit documented.

Clinical cure rates at EOT were 93.2% (328/352) and 95.1% (330/347) in the moxifloxacin and ertapenem groups, respectively, in the PP population (95% CI: -5.0 to 1.9).

Similar results were observed in the ITT population.

Bacteriological Response

The total number of subjects valid for efficacy with pre-therapy intraabdominal and/or blood pathogens was 297 in the moxifloxacin group and 276 in the ertapenem group. Ten (10) and 3 subjects in the moxifloxacin and ertapenem groups, respectively, had blood isolates. One subject in each group had blood isolates only. A vast majority of the PP subjects had a polymicrobial infection, i.e., 85% (252/297) of the moxifloxacin-treated subjects compared with 84% (232/276) of the comparator-treated subjects.

The bacteriological success rates at the TOC visit in the PP/MBE population were comparable in both the moxifloxacin group (87%) and the ertapenem group (90%) (95% CI: -9.0% to 1.5%). In the ITT/MBE population, the bacteriological success rate was 80% in the moxifloxacin group and 84% in the ertapenem group (95 % CI -10.0% to 1.5%); see Table 4.

The bacteriological response rates observed at the TOC visit are presented for the PP/MBE and ITT/MBE populations in Table 4.

Table 4: Bacteriological response rates at the TOC visit (PP/MBE and ITT/MBE populations)

PP/MBE	Moxifloxacin (N=297) n (%)	Ertapenem (N=276) n (%)	95% CI
Bacteriological success	257 (86.5)	249 (90.2)	-9.0 to 1.5
Presumed eradication	257 (86.5)	249 (90.2)	
Bacteriological non-success	40 (13.5)	27 (9.8)	
Persistence	20 (6.7)	9 (3.3)	
Presumed persistence	20 (6.7)	18 (6.5)	
ITT/MBE	Moxifloxacin (N=340) n (%)	Ertapenem (N=308) n (%)	95% CI
Bacteriological success	271 (79.7)	258 (83.8)	-10.0 to 1.5
Presumed eradication	271 (79.7)	258 (83.8)	
Bacteriological non-success	69 (20.3)	50 (16.2)	
Persistence	23 (6.8)	9 (2.9)	
Presumed persistence	23 (6.8)	19 (6.2)	
Indeterminate	23 (6.8)	22 (7.1)	

Bacteriological success includes presumed eradication without recurrence, super-, or reinfection. Persistence includes persistence with super- or reinfections.

For the calculation of confidence intervals indeterminate/missing responses were treated as non-successes

Bacteriological success rates in bacteremic of the per protocol population subjects were 70.0% (7/10) and 66.7% (2/3) for the moxifloxacin and ertapenem groups, respectively.

Table 5 presents bacteriological response at the TOC visit by most frequently isolated intra-abdominal organisms (only the most frequently isolated intra-abdominal organisms identified at baseline are presented).

Table 5: Bacteriological response by most frequent (N≥10) causative intra-abdominal organisms and by number of subjects at the TOC visit (PP/MBE population)

Group Genus/*Species*	Bacteriological Response	Moxifloxacin n/N (%)	Ertapenem n/N (%)	Total n/N (%)
Organisms	Eradication[a]	1/1018 (0.1)	0/909 (0)	1/1927 (<1)
	Presumed eradication	858/1018 (84.3)	813/909 (89.4)	1671/1927 (86.7)
	Persistence	40/1018 (3.9)	13/909 (1.4)	53/1927 (2.8)
	Presumed persistence	119/1018 (11.7)	83/909 (9.1)	202/1927 (10.5)
Subjects	No organisms[1]	1/297 (0.3)	1/276 (0.3)	2/573 (<1)
	Presumed eradication	256/297 (86.2)	248/276 (89.9)	504/573 (88.0)
	Persistence	20/297 (6.7)	9/276 (3.3)	29/573 (5.1)
	Presumed persistence	20/297 (6.7)	18/276 (6.5)	38/573 (6.6)
Gram-positive cocci aerobic				
Organisms	Presumed eradication	259/311 (83.3)	244/275 (88.7)	503/586 (85.8)
	Persistence	9/311 (2.9)	6/275 (2.2)	15/586 (2.6)
	Presumed persistence	43/311 (13.8)	25/275 (9.1)	68/586 (11.6)
Subjects	Presumed eradication	181/210 (86.2)	171/192 (89.1)	352/402 (87.6)
	Persistence	7/210 (3.3)	6/192 (3.1)	13/402 (3.2)
	Presumed persistence	22/210 (10.5)	15/192 (7.8)	37/402 (9.2)
S. aureus, methicillin susceptible				
by organism	Presumed eradication	10/10 (100.0)	5/5 (100.0)	15/15 (100.0)
by subject	Presumed eradication	10/10 (100.0)	5/5 (100.0)	15/15 (100.0)
S. salivarius				
by organism	Presumed eradication	13/13 (100.0)	13/13 (100.0)	26/26 (100.0)
by subject	Presumed eradication	12/12 (100.0)	13/13 (100.0)	25/25 (100.0)
S. anginosus				
by organism	Presumed eradication	60/74 (81.1)	62/69 (89.9)	122/143 (85.3)
	Persistence	4/74 (5.4)	2/69 (2.9)	6/143 (4.2)
	Presumed persistence	10/74 (13.5)	5/69 (7.2)	15/143 (10.5)
by subject	Presumed eradication	56/67 (83.6)	57/64 (89.1)	113/131 (86.3)
	Persistence	4/67 (6.0)	2/64 (3.1)	6/131 (4.6)
	Presumed persistence	7/67 (10.4)	5/64 (7.8)	12/131 (9.2)
S. constellatus				
by organism	Presumed eradication	43/51 (84.3)	40/42 (95.2)	83/93 (89.2)
	Persistence	2/51 (3.9)	0/42 (0)	2/93 (2.2)
	Presumed persistence	6/51 (11.8)	2/42 (4.8)	8/93 (8.6)
by subject	Presumed eradication	42/50 (84.0)	37/39 (94.9)	79/89 (88.8)
	Persistence	2/50 (4.0)	0/39 (0)	2/89 (2.2)
	Presumed persistence	6/50 (12.0)	2/39 (5.1)	8/89 (9.0)

Table 5 continued: Bacteriological response by most frequent (N≥10) causative intra-abdominal organisms and by number of subjects at the TOC visit (PP/MBE population)

Group Genus/*Species*	Bacteriological Response	Moxifloxacin n/N (%)	Ertapenem n/N (%)	Total n/N (%)
S. parasanguis				
by organism	Presumed eradication	7/8 (87.5)	7/7 (100.0)	14/15 (93.3)
	Presumed persistence	1/8 (12.5)	0/7 (0)	1/15 (6.7)
by subject	Presumed eradication	7/8 (87.5)	5/5 (100.0)	12/13 (92.3)
	Presumed persistence	1/8 (12.5)	0/5 (0)	1/13 (7.7)
S. oralis				
by organism	Presumed eradication	15/17 (88.2)	16/18 (88.9)	31/35 (88.6)
	Presumed persistence	2/17 (11.8)	2/18 (11.1)	4/35 (11.4)
by subject	Presumed eradication	11/13 (84.6)	15/17 (88.2)	26/30 (86.7)
	Presumed persistence	2/13 (15.4)	2/17 (11.8)	4/30 (13.3)
S. bovis				
by organism	Presumed eradication	4/4 (100.0)	4/6 (66.7)	8/10 (80.0)
	Presumed persistence	0/4 (0)	2/6 (33.3)	2/10 (20.0)
by subject	Presumed eradication	4/4 (100.0)	4/6 (66.7)	8/10 (80.0)
	Presumed persistence	0/4 (0)	2/6 (33.3)	2/10 (20.0)
E. faecalis				
by organism	Presumed eradication	29/35 (82.9)	29/36 (80.6)	58/71 (81.7)
	Persistence	0/35 (0)	3/36 (8.3)	3/71 (4.2)
	Presumed persistence	6/35 (17.1)	4/36 (11.1)	10/71 (14.1)
by subject	Presumed eradication	29/35 (82.9)	28/35 (80.0)	57/70 (81.4)
	Persistence	0/35 (0)	3/35 (8.6)	3/70 (4.3)
	Presumed persistence	6/35 (17.1)	4/35 (11.4)	10/70 (14.3)
E. faecium				
by organism	Presumed eradication	20/25 (80.0)	16/19 (84.2)	36/44 (81.8)
	Persistence	2/25 (8.0)	0/19 (0)	2/44 (4.5)
	Presumed persistence	3/25 (12.0)	3/19 (15.8)	6/44 (13.6)
by subject	Presumed eradication	19/24 (79.2)	16/19 (84.2)	35/43 (81.4)
	Persistence	2/24 (8.3)	0/19 (0)	2/43 (4.7)
	Presumed persistence	3/24 (12.5)	3/19 (15.8)	6/43 (14.0)
E. avium				
by organism	Presumed eradication	12/16 (75.0)	16/21 (76.2)	28/37 (75.7)
	Persistence	0/16 (0)	1/21 (4.8)	1/37 (2.7)
	Presumed persistence	4/16 (25.0)	4/21 (19.0)	8/37 (21.6)
by subject	Presumed eradication	12/16 (75.0)	16/21 (76.2)	28/37 (75.7)
	Persistence	0/16 (0)	1/21 (4.8)	1/37 (2.7)
	Presumed persistence	4/16 (25.0)	4/21 (19.0)	8/37 (21.6)
Gram-positive rods anaerobic Organisms	Presumed eradication	13/14 (92.9)	15/16 (93.8)	28/30 (93.3)
	Presumed persistence	1/14 (7.1)	1/16 (6.3)	2/30 (6.7)
Subjects	Presumed eradication	13/14 (92.9)	12/13 (92.3)	25/27 (92.6)
	Presumed persistence	1/14 (7.1)	1/13 (7.7)	2/27 (7.4)

Table 5 continued: Bacteriological response by most frequent (N≥10) causative intra-abdominal organisms and by number of subjects at the TOC visit (PP/MBE population)

Group Genus/*Species*	Bacteriological Response	Moxifloxacin n/N (%)	Ertapenem n/N (%)	Total n/N (%)
C. perfringens				
by organism	Presumed eradication	6/6 (100.0)	8/8 (100.0)	14/14 (100.0)
by subject	Presumed eradication	6/6 (100.0)	7/7 (100.0)	13/13 (100.0)
Gram-neg rods fermentative				
Organisms	Eradication	1/442 (<1)	0/375 (0)	1/817 (<1)
	Presumed eradication	381/442 (86.2)	336/375 (89.6)	717/817 (87.8)
	Persistence	19/442 (4.3)	5/375 (1.3)	24/817 (2.9)
	Presumed persistence	41/442 (9.3)	34/375 (9.1)	75/817 (9.2)
Subject	Presumed eradication	207/238 (87.0)	198/218 (90.8)	405/456 (88.8)
	Persistence	13/238 (5.5)	5/218 (2.3)	18/456 (3.9)
	Presumed persistence	18/238 (7.6)	15/218 (6.9)	33/456 (7.2)
E. coli, non-ESBL				
by organism	Presumed eradication	232/264 (87.9)	209/233 (89.7)	441/497 (88.7)
	Persistence	14/264 (5.3)	4/233 (1.7)	18/497 (3.6)
	Presumed persistence	18/264 (6.8)	20/233 (8.6)	38/497 (7.6)
by subject	Presumed eradication	172/196 (87.8)	165/182 (90.7)	337/378 (89.2)
	Persistence	11/196 (5.6)	4/182 (2.2)	15/378 (4.0)
	Presumed persistence	13/196 (6.6)	13/182 (7.1)	26/378 (6.9)
K. pneumoniae, non-ESBL				
by organism	Presumed eradication	20/23 (87.0)	21/24 (87.5)	41/47 (87.2)
	Persistence	1/23 (4.3)	0/24 (0)	1/47 (2.1)
	Presumed persistence	2/23 (8.7)	3/24 (12.5)	5/47 (10.6)
by subject	Presumed eradication	20/23 (87.0)	17/20 (85.0)	37/43 (86.0)
	Persistence	1/23 (4.3)	0/20 (0)	1/43 (2.3)
	Presumed persistence	2/23 (8.7)	3/20 (15.0)	5/43 (11.6)
K. oxytoca, non-ESBL				
by organism	Presumed eradication	22/26 (84.6)	14/16 (87.5)	36/42 (85.7)
	Presumed persistence	4/26 (15.4)	2/16 (12.5)	6/42 (14.3)
by subject	Presumed eradication	20/23 (87.0)	13/15 (86.7)	33/38 (86.8)
	Presumed persistence	3/23 (13.0)	2/15 (13.3)	5/38 (13.2)
P. mirabilis, non-ESBL				
by organism	Presumed eradication	10/13 (76.9)	5/6 (83.3)	15/19 (78.9)
	Persistence	3/13 (23.1)	0/6 (0)	3/19 (15.8)
	Presumed persistence	0/13 (0)	1/6 (16.7)	1/19 (5.3)
by subject	Presumed eradication	10/12 (83.3)	5/6 (83.3)	15/18 (83.3)
	Persistence	2/12 (16.7)	0/6 (0)	2/18 (11.1)
	Presumed persistence	0/12 (0)	1/6 (16.7)	1/18 (5.6)

Table 5 continued: Bacteriological response by most frequent (N≥10) causative intra-abdominal organisms and by number of subjects at the TOC visit (PP/MBE population)

Group Genus/*Species*	Bacteriological Response	Moxifloxacin n/N (%)	Ertapenem n/N (%)	Total n/N (%)
E. cloacae, non-ESBL				
by organism	Presumed eradication	9/10 (90.0)	5/6 (83.3)	14/16 (87.5)
	Presumed persistence	1/10 (10.0)	1/6 (16.7)	2/16 (12.5)
by subject	Presumed eradication	7/8 (87.5)	5/6 (83.3)	12/14 (85.7)
	Presumed persistence	1/8 (12.5)	1/6 (16.7)	2/14 (14.3)
C. freundii, non-ESBL				
by organism	Presumed eradication	9/12 (75.0)	15/16 (93.8)	24/28 (85.7)
	Presumed persistence	3/12 (25.0)	1/16 (6.3)	4/28 (14.3)
by subject	Presumed eradication	8/10 (80.0)	13/14 (92.9)	21/24 (87.5)
	Presumed persistence	2/10 (20.0)	1/14 (7.1)	3/24 (12.5)
M. morganii, non-ESBL				
by organism	Presumed eradication	5/6 (83.3)	8/8 (100.0)	13/14 (92.9)
	Presumed persistence	1/6 (16.7)	0/8 (0)	1/14 (7.1)
by subject	Presumed eradication	5/6 (83.3)	8/8 (100.0)	13/14 (92.9)
	Presumed persistence	1/6 (16.7)	0/8 (0)	1/14 (7.1)
P. aeruginosa				
by organism	Presumed eradication	36/40 (90.0)	20/21 (95.2)	56/61 (91.8)
	Persistence	1/40 (2.5)	0/21 (0)	1/61 (1.6)
	Presumed persistence	3/40 (7.5)	1/21 (4.8)	4/61 (6.6)
by subject	Presumed eradication	32/35 (91.4)	17/18 (94.4)	49/53 (92.5)
	Persistence	1/35 (2.9)	0/18 (0)	1/53 (1.9)
	Presumed persistence	2/35 (5.7)	1/18 (5.6)	3/53 (5.7)
Gram-negative rods anaerobic				
Organisms	Presumed eradication	202/247 (81.8)	215/240 (89.6)	417/487 (85.6)
	Persistence	12/247 (4.9)	2/240 (<1)	14/487 (2.9)
	Presumed persistence	33/247 (13.4)	23/240 (9.6)	56/487 (11.5)
Subjects	Presumed eradication	145/172 (84.3)	144/160 (90.0)	289/332 (87.0)
	Persistence	11/172 (6.4)	2/160 (1.3)	13/332 (3.9)
	Presumed persistence	16/172 (9.3)	14/160 (8.8)	30/332 (9.0)
B. distasonis				
by organism	Presumed eradication	15/17 (88.2)	12/13 (92.3)	27/30 (90.0)
	Presumed persistence	2/17 (11.8)	1/13 (7.7)	3/30 (10.0)
by subject	Presumed eradication	15/17 (88.2)	12/13 (92.3)	27/30 (90.0)
	Presumed persistence	2/17 (11.8)	1/13 (7.7)	3/30 (10.0)
B. fragilis				
by organism	Presumed eradication	71/90 (78.9)	87/95 (91.6)	158/185 (85.4)
	Persistence	9/90 (10.0)	2/95 (2.1)	11/185 (5.9)
	Presumed persistence	10/90 (11.1)	6/95 (6.3)	16/185 (8.6)
by subject	Presumed eradication	70/87 (80.5)	83/90 (92.2)	153/177 (86.4)
	Persistence	9/87 (10.3)	2/90 (2.2)	11/177 (6.2)
	Presumed persistence	8/87 (9.2)	5/90 (5.6)	13/177 (7.3)

Table 5 continued: Bacteriological response by most frequent (N≥10) causative intra-abdominal organisms and by number of subjects at the TOC visit (PP/MBE population)

Group Genus/*Species*	Bacteriological Response	Moxifloxacin n/N (%)	Ertapenem n/N (%)	Total n/N (%)
B. ovatus				
by organism	Presumed eradication	19/25 (76.0)	14/14 (100.0)	33/39 (84.6)
	Persistence	1/25 (4.0)	0/14 (0)	1/39 (2.6)
	Presumed persistence	5/25 (20.0)	0/14 (0)	5/39 (12.8)
by subject	Presumed eradication	18/24 (75.0)	14/14 (100.0)	32/38 (84.2)
	Persistence	1/24 (4.2)	0/14 (0)	1/38 (2.6)
	Presumed persistence	5/24 (20.8)	0/14 (0)	5/38 (13.2)
B. thetaiotaomicron				
by organism	Presumed eradication	37/45 (82.2)	51/54 (94.4)	88/99 (88.9)
	Persistence	1/45 (2.2)	0/54 (0)	1/99 (1.0)
	Presumed persistence	7/45 (15.6)	3/54 (5.6)	10/99 (10.1)
by subject	Presumed eradication	36/43 (83.7)	47/50 (94.0)	83/93 (89.2)
	Persistence	1/43 (2.3)	0/50 (0)	1/93 (1.1)
	Presumed persistence	6/43 (14.0)	3/50 (6.0)	9/93 (9.7)
B. uniformis				
by organism	Presumed eradication	10/11 (90.9)	20/23 (87.0)	30/34 (88.2)
	Presumed persistence	1/11 (9.1)	3/23 (13.0)	4/34 (11.8)
by subject	Presumed eradication	10/11 (90.9)	20/23 (87.0)	30/34 (88.2)
	Presumed persistence	1/11 (9.1)	3/23 (13.0)	4/34 (11.8)
B. vulgatus				
by organism	Presumed eradication	15/16 (93.8)	9/11 (81.8)	24/27 (88.9)
	Presumed persistence	1/16 (6.3)	2/11 (18.2)	3/27 (11.1)
by subject	Presumed eradication	15/16 (93.8)	9/11 (81.8)	24/27 (88.9)
	Presumed persistence	1/16 (6.3)	2/11 (18.2)	3/27 (11.1)
P. buccae				
by organism	Presumed eradication	6/8 (75.0)	1/6 (16.7)	7/14 (50.0)
	Presumed persistence	2/8 (25.0)	5/6 (83.3)	7/14 (50.0)
by subject	Presumed eradication	5/7 (71.4)	1/5 (20.0)	6/12 (50.0)
	Presumed persistence	2/7 (28.6)	4/5 (80.0)	6/12 (50.0)

[a] one subject in each treatment group had only a positive blood culture pre therapy

There were no major differences in bacteriological response by bacterial grouping or species.

Moxifloxacin resistance was fairly common among the persisting/presumably persisting organisms. Among the non-ESBL producing strains of *E. coli*, which persisted at TOC, 4 (out of 32) were in-vitro resistant (moxifloxacin's MIC > 2 mg/L) at baseline. Three (out of 19) persisting *B. fragilis* strains were in-vitro resistant.

In both treatment groups, the bacteriological eradication/presumed eradication rate at the TOC visit was higher in subjects with monomicrobial infections (95.6% in the moxifloxacin group, 97.7% in the ertapenem group) than in subjects with polymicrobial infections (84.9% in the moxifloxacin group, 88.8% in the ertapenem group).

Bacteriological success rates at the during therapy visit were 58.9% (175/297) and 55.8% (154/276) in the moxifloxacin and ertapenem groups, respectively (95% CI: -5.0 to 10.3). A high number of subjects in each group had an indeterminate bacteriological response (moxifloxacin, 106 [35.7%], ertapenem, 112 [40.6%]), mainly because of unavailable bacterial culture.

Bacteriological success rates at EOT were similar in the two treatment groups: 88.2% (262/297) in the moxifloxacin group and 92.0% in the ertapenem group (254/276), 95% CI: -8.8 to 1.0.

Mortality

Mortality attributable to intra-abdominal infection was a secondary efficacy parameter. The rates of death due to infection in the ITT population were 2.0% (8/408) in the moxifloxacin group and 0.5% (2/390) in the ertapenem group, p=0.62. In the PP population, they were 0.9% (3/352) and 0.3% (1/347) in the moxifloxacin and ertapenem groups, respectively, p=0.11.

Results Summary — Safety

Adverse events

More than half of all subjects in the safety population experienced treatment-emergent AEs (TEAEs). The incidence was higher in the moxifloxacin group (239 subjects [59%]) than in the ertapenem group (200 subjects [51%]), (p=0.04).

The highest rates of TEAEs were from the system organ classes (SOCs) of infections and infestations (moxifloxacin 22%; ertapenem 16%), gastrointestinal disorders (moxifloxacin 21%; ertapenem 15%) and investigations (moxifloxacin 15%; ertapenem 14%). The most commonly reported treatment-emergent AEs were wound infections (moxifloxacin 12%; ertapenem 7%), nausea (moxifloxacin 8%; ertapenem 4%), and increased lipase (6% in both the groups).

Drug-related AEs were experienced by the same proportion of subjects: 77 (19%) subjects in the moxifloxacin group and 74 subjects [19%] in the ertapenem group. By SOC, the most frequent drug-related treatment-emergent AEs were investigations (moxifloxacin 9%; ertapenem 10%). Of these, the most frequent were increased lipase (moxifloxacin 3%; ertapenem 5%) and gamma glutamyl transpeptidase (GGT), (moxifloxacin 3%; ertapenem 4%).

Severe TEAEs occurred infrequently, and at a similar incidence in both treatment groups (moxifloxacin 9%; ertapenem 8%, p= 0.62). Severe drug-related TEAEs were reported for 1% of subjects in the moxifloxacin group and 2% of subjects in the ertapenem group. The most frequent severe drug-related TEAEs were recorded within the SOCs of investigations (3 subjects in the ertapenem group [GGT increase in 2 subjects, lipase increase in 1 subject] and none in the moxifloxacin group) and of gastrointestinal disorders (2 subjects in the moxifloxacin group [1 subject with nausea, 1 with nausea and vomiting] and 1 subject in the ertapenem group with peritonitis).

Twenty two (22) subjects in the moxifloxacin group and 12 subjects in the ertapenem group died. Four deaths occurred during treatment (3 subjects in the moxifloxacin group and 1 subject in the ertapenem group) and 30 deaths occurred after the end of treatment (19 subjects in the moxifloxacin group and 11 subjects in the ertapenem group). No deaths in the moxifloxacin group were considered to be related to the study treatment, whereas 1 death in the ertapenem group was considered to be related to study treatment (one subject discontinued medication due to lack of drug effect, developed subsequent septic shock and died due to severe multi organ failure 6 days after completing study treatment).

Serious adverse events, discontinuations and hospitalizations due to AEs

Serious treatment-emergent AEs were observed in 60 subjects (15%) in the moxifloxacin and 48 subjects (12%) in the ertapenem group. Fifteen (15) subjects experienced treatment-emergent, drug-related SAEs (9 [2%] in the moxifloxacin group and 6 [2%] in the ertapenem

group). Seven subjects experienced severe treatment-emergent, drug related SAEs (3 [1%] in the moxifloxacin group, and 4 [1%] in the ertapenem group). Premature terminations due to AEs (moxifloxacin 3%; ertapenem 2%) and hospitalizations or prolonged hospitalizations (10% in each group) were observed in a similar number of subjects in the two treatment groups.

Other significant AEs

There was no clear evidence of any treatment effect on the incidence of hepatic or cardiac events. In the SOC of infections and infestations, one subject in each treatment group experienced a drug-related clostridial infection (*Clostridium difficile* colitis), requiring permanent discontinuation of treatment for the subject in the moxifloxacin group.

Clinical laboratory evaluations

There were no clinically significant differences between the treatment groups with regard to the clinically significant changes of laboratory parameters analyzed with the exception of alkaline phosphatase, which occurred slightly more frequently in the moxifloxacin group (25%) than the ertapenem group (17%). Clinically significant hematology abnormalities were generally infrequent.

Vital signs

The observed decrease in heart rate, respiratory rate and temperature from baseline to EOT and TOC were considered clinically relevant but expected for this subject population. Overall, mean values for vital signs were unremarkable and raised no safety concerns.

Conclusions

The study demonstrated that treatment with moxifloxacin 400 mg IV once daily was not less effective than treatment with the comparator ertapenem, 1.0 g IV once daily in adults with cIAIs. In the PP population, the lower limit of the 95% CI of the difference between the two clinical success rates (moxifloxacin minus ertapenem group) at the TOC visit was greater than -10% and the null hypothesis of inferiority could be rejected. Efficacy results in other populations analyzed, i.e., ITT, PP/MBE and ITT/MBE, support those of the primary efficacy population in demonstrating noninferiority of moxifloxacin versus ertapenem.

Drug-related AEs were experienced by the same proportion of subjects in both groups and the nature of AEs was as expected in this cIAI population. There was no significant difference in the occurrence of SAEs.

Publication(s):	De Waele JJ, Tellado JM, Alder J, Reimnitz P, Jensen M, Hampel B, Arvis P. Randomised clinical trial of moxifloxacin versus ertapenem in complicated intra-abdominal infections: results of the PROMISE study. Int J Antimicrob Agents. 2013 Jan;41(1):57-64. doi: 10.1016/j.ijantimicag.2012.08.013. Epub 2012 Nov 13. PMID: 23153963		
Date Created or Date Last Updated:	21 MAY 2013	**Date of Clinical Study Report:**	26 JAN 2010

Investigational Site List

Marketing Authorization Holder in Germany	
Name	Bayer Vital GmbH
Postal Address	D-51368 Leverkusen, Germany
Sponsor in Germany (if applicable)	
Legal Entity Name	Bayer HealthCare AG
Postal Address	D-51368 Leverkusen, Germany

List of Investigational Sites

No	Facility Name	Street	ZIP Code	City	Country
1	Hospital Central	Salta y Alem		Mendoza	ARGENTINA
2	Hospital de Agudos "Dr. Carlos Bocalandro"	Ruta 8, N°. 9100 (Km 20,900)	1657	3 de Febrero	ARGENTINA
3	Hospital de Emergencias Clemente Alvarez	Gral. Benjamín Virasoro 1100		Rosario	ARGENTINA
4	Hospital Zonal General de Agudo 'Dr. Ramón Carrillo	Infectious Diseases Hipolito Irigoyen	B1702FWM	Ciudadela	ARGENTINA
5	Hospital Zonal General de Agudos 'Heroes de Malvinas'	Infectious Diseases Av. Balbín 1910	B1712FJN	Merlo	ARGENTINA
6	Hosp. Municipal de Agudos "Mi Pueblo"	Progreso 240	1888	Florencio Varela	ARGENTINA
7	Nuevo Hospital San Roque	Bajada Pucará 1900	5000	Córdoba	ARGENTINA
8	Sanatorio Güemes	Fco. Acuña de Figueroa 1240	C1180AAX	Buenos Aires	ARGENTINA

9	Sanatorio San José	Sánchez de Bustamante 1674		Capital Federal	ARGENTINA
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11	UZ Brussel	Laarbeeklaan 101	1090	BRUXELLES - BRUSSEL	BELGIUM
12	UZ Gent	De Pintelaan 185	9000	GENT	BELGIUM
13	MHAT Russe	Surgery Department II 2 "Nezavisimost"str.	7002	Rousse	BULGARIA
14	Military Medical Academy	3 Georgi Sofiiski blvd.	1431	Sofia	BULGARIA
15	Multiprofile Hospital for Active Treatment and Emergency Med	Macedonia blvd. 21	1606	Sofia	BULGARIA
16	UMHAT Dr. Georgi Stranski	Georgi Kotchev str. 8A	5800	Pleven	BULGARIA
17	Ida-Viru Central Hospital	Ravi 10 Kohtla-Jarve 30322 Estonia	30322	Kohtla-Jarve	ESTONIA
18	Regional Hospital of North Estonia	Sutiste 1	EE-13419	Tallin	ESTONIA
19	Tartu University Clinics	Puusepa str. 8	EE-51014	Tartu	ESTONIA
20	Centre Hospitalier Montargoise - Amilly Cedex	Centre Hospitalier Montargoise Service de Chirurgie visc. et urologie 658 rue des Bourgoins	45207	AMILLY CEDEX	FRANCE

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24	Kreiskrankenhaus Beeskow	Schützenstr. 28	15848	Beeskow	GERMANY
25	Universitätskliniken des Saarlandes	Klinik für Allgemeine Chirurgie, Viszeral-, Gefäß- und Kinderchirurgie Kirrberger Straße	66424	Homburg	GERMANY
26	Universitätsklinikum Heidelberg	Chirurgische Universitätsklinik Allgemeine, Viszerale, Unfallchirurgie und Poliklinik Im Neuenheimer Feld 110	69120	Heidelberg	GERMANY
27	University General Hospital of Patras	Department of Internal Medicine Infectious Disease	265 00	Rio Patras	GREECE
28	Bnai Zion Medical Center	47, Golomb Street P.O.B. 4940	31048	Haifa	ISRAEL
29	Meir Medical Center	Clalit Health Services 59, Tchernichovsky Street	44281	Kfar Saba	ISRAEL

30	Central Hospital of Liepaja	Slimnicas street 25	3402	Liepaja	LATVIA
31	Daugavpils Regional Hospital	Vasarnicas 20	LV-5417	Daugavpils	LATVIA
32	Paula Stradina Kliniskas Universitates slimnica	Pilsonu iela 13	1002	Riga	LATVIA
33	Rezekne Hospital	11 Novembra Str. 41		Rezekne	LATVIA
34	Riga Clinical Hospital "Gailezers"	2, Hipokrata Str.	LV-1038	Riga	LATVIA
35	Valmiera Hospital	Jumaras street 195	LV-4201	Valmiera	LATVIA
36	Kaunas District Hospital	Hipodromo str. 13	45130	Kaunas	LITHUANIA
37	Klaipeda District Hospital	S.Neries 3	LT-92231	Klaipeda	LITHUANIA
38	University Hospital of Vilnus City	Antakalnio 57	10207	Vilnius	LITHUANIA
39	Vilnius University Hospital of Emergency Care	Siltnamiu 29	LT-04130	Vilnius	LITHUANIA
40	Clinical Emergency County Hospital	Surgery Clinic no 1 Clinicilor str 3-5	400006	Cluj-Napoca	ROMANIA
41	County Clinical Hospital	Gheoghe Doja str. 65		Oradea	ROMANIA
42	County Clinical Hospital	Calea Bucuresti str 25-27		Brasov	ROMANIA
43	Fundeni Clinical Institute	Fundeni str 258, Sector 2		Bucharest	ROMANIA
44	University Country Hospital	I. Bulbuca str. 156	300748	Timisoara	ROMANIA
45	1st Medical Academy Municipal Hospital N61	Dovatora 15	119048	Moscow	RUSSIA
46	City Clinical Hospital no 13	Velozavodskaya 1/1	115280	Moscow	RUSSIA

47	Smolensk Medical Academy	based on Regional Clinical Hospital Krupskoj str. 28	214019	Smolensk	RUSSIA
48	Pretoria Academic Hospital Ethics Committee	Department of Surgery Faculty of Health Sciences Pretoria Academic Hospital Dr Savage Road	0001	Pretoria	SOUTH AFRICA
49	University of Stellenbosch	PROF WARREN DEPARTMENT OF SURGERY (GENERAL) MEDICAL SCHOOL FRANCIE VAN ZIJL DRIVE PARROW	7500	CAPE TOWN	SOUTH AFRICA
50	Vergelegen Medi-Clinic	Main Road	7130	Somerset West	SOUTH AFRICA
51	Ciutat Sanitària i Universitària de Bellvitge	Servicio de Medicina Intensiva (Planta 1) c/Feixa Llarga s/n	08907	L'Hospitalet de Llobregat	SPAIN
52	Hospital General Universitario Gregorio Marañón	Servicio de Cirugía, Area 2200 C/ Dr. Esquerdo, 46	28007	Madrid	SPAIN

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Avelox [i.v]
Brand/Trade Name(s) ex-US	Actira®, Avalox®, Avelox®, Izilox®, Megaxin®, Octegra® , Proflox®
Generic Name	Moxifloxacin
Main Product Company Code	BAY12-8039
Other Company Code(s)	n/a
Chemical Description	1-Cyclopropyl-6-fluoro-8-methoxy-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.
Other Product Aliases	n/a

Date of last Update/Change: 11 September 2013