SUPPLEMENTARY MATERIAL

APPENDIX 1. Criteria for Preoperative Enrollment

The following clinical criteria were to be met at screening, and the subject's infection was to be confirmed by surgical intervention within 24 hours of entry:

1) Evidence of a systemic inflammatory response, with at least 1 of the following:

a) Fever (defined as ≥38.0°C [≥100.4°F] orally OR an oral equivalent [≥38.5°C (≥101.3°F) by tympanic or rectal measurement])

b) Elevated WBC (≥10,500/mm^3)

c) Drop in blood pressure (systolic blood pressure <90 mm Hg without need for pressor support)

d) Increased pulse and respiratory rates

e) Hypoxemia

f) Altered mental status

AND

2) At least 1 physical finding consistent with IAI, such as:

a) Abdominal pain and/or tenderness

b) Localized or diffuse abdominal wall rigidity

c) Abdominal mass

d) Ileus

AND

3) Supportive radiologic findings, such as intraperitoneal abscess, detected by abdominal CT scan

AND

4) Requirement for surgical intervention, including open laparotomy, percutaneous drainage of an abscess, or laparoscopic surgery.

Specimens from the surgical intervention, once performed, must have been sent for aerobic and anaerobic culture and susceptibility testing. Only subjects with an intraoperative culture positive for the presence of at least 1 Gram-negative enteric(s) and/or anaerobic pathogen(s) commonly isolated in IAI were considered microbiologically evaluable.

APPENDIX 2. Assessment of Response

1. Clinical Response

Clinical (abdominal) signs and symptoms of complicated IAI, including fever (or history of fever), chills, abdominal pain, nausea, vomiting, tenderness to palpation, rebound tenderness, guarding, mass, and ascites were determined at study entry, during IV study therapy (Day 3), at the end of IV study therapy (DCIV), at the EFU visit (5 to 9 days posttherapy), at the GFU visit (Day 28 [+ 7 days] days post-randomization), and at the LFU visit (28 to 42 days posttherapy). Signs and symptoms were graded for intensity by the investigator as none, mild, moderate, or severe. Other pertinent findings were recorded including the ability to take enteral feeding and passage of gas or stool. Clinical response assessments were performed at the DCIV, EFU, and LFU visits.

1.1. Clinical Response at the DCIV Visit

At the DCIV visit, the investigator assessed the clinical response as "cure", "failure", or "indeterminate" based on comparison to signs and symptoms at study entry. A favorable clinical response rating at the DCIV visit is "cure." An unfavorable clinical response rating is "failure."

A patient whose clinical symptoms had improved at any given time point, but who had not yet achieved a "cure" was determined a "failure" until he/she had achieved a "cure." Patients with a clinical response rating of "indeterminate" were excluded from the clinical response assessments in the microbiologically-evaluable population for the DCIV visit; however, such patients were counted as having an unfavorable clinical response for the DCIV visit in the microbiological intention to treat (MITT) population. Reason for failure at the DCIV visit was indicated according to clinical response definitions outlined in Table 1.

Table 1
Definitions of Clinical Response at the DCIV Visit

Clinical Response	Response Definition
Cure	All or most pretherapy signs and symptoms of the index infection have resolved (or returned to "preinfection status") AND no additional antibiotic therapy is required.
Failure	No apparent response to IV study therapy in prestudy signs and symptoms, as documented by persistence or progression of most or all pretherapy signs and symptoms; can also include any of the following: (a) Death related to the intra-abdominal infection at any time point; **OR** (b) Persisting or recurrent infection within the abdomen documented by the findings at re-intervention either percutaneously or operatively; **OR** (c) Evidence of a postsurgical wound infection; **OR** (d) Use of additional (non-study) antibacterial drug therapy for the baseline or a new intra-abdominal infection
Indeterminate	Study data are not available for evaluation of clinical response for any reasons at the DCIV visit, including: (a) Complication related to underlying medical condition; **OR** (b) Patient was withdrawn for any reason before sufficient data had been obtained to permit evaluation of clinical response; **OR** (c) Extenuating circumstances preclude classification as "cure" or "failure" (d) Death occurred during the study period and the index infection was clearly noncontributory

APPENDIX 2. Assessment of Response

1.2. Clinical Response at the EFU Visit

At the posttherapy visit 5 to 9 days after the completion of IV study therapy (EFU), the investigator assessed the clinical response as "cure", "failure", or "indeterminate**"** based on comparison to signs and symptoms at study entry (Table 2). A favorable clinical response rating at the EFU visit was "cure." An unfavorable clinical response rating at the EFU visit was "failure."

Patients with a clinical response rating of "indeterminate" at the EFU visit were excluded from the microbiologically evaluable population with respect to the clinical response endpoint.

Table 2
Definitions of Clinical Response at the EFU Visit

Clinical Response	Response Definition
Cure	All or most pretherapy signs and symptoms of the index infection have resolved (or returned to "preinfection status") AND no additional antibiotic therapy is/was required.
Failure	No apparent response to IV study therapy in prestudy signs and symptoms, as documented by persistence or progression of most or all pretherapy signs and symptoms. This apparent lack of response can also include any of the following: (a) Death related to the intra-abdominal infection at any time point; **OR** (b) Persisting or recurrent infection within the abdomen documented by the findings at re-intervention either percutaneously or operatively; **OR** (c) Evidence of a postsurgical wound infection; **OR** (d) Use of additional (non-study) antibacterial drug therapy for the baseline or a new intra-abdominal infection
Indeterminate	Study data are not available for evaluation of clinical response for any reasons at the EFU visit, including: (a) Complication related to underlying medical condition (b) Patient was withdrawn for any reason before sufficient data had been obtained to permit evaluation of clinical response (c) Extenuating circumstances preclude classification as "cure" or "failure" (d) Death occurred during the study period and the index infection was clearly noncontributory

APPENDIX 2. Assessment of Response

1.3. Clinical Response at the LFU Visit

At the post-therapy visit 28 to 42 days after the completion of IV study therapy (LFU), the investigator assessed the clinical response as "sustained cure," "failure," "relapse," or "indeterminate" based on comparison to admission signs and symptoms (Table 3). A favorable clinical response rating at the LFU visit was "sustained cure." An unfavorable clinical response rating at the LFU visit was "failure" or "relapse."

Patients with a clinical response rating of "indeterminate" at the LFU visit were excluded from the microbiologically evaluable population with respect to the clinical response endpoint.

Table 3
Definitions of Clinical Response at the LFU Visit

Clinical Response	Response Definition
Sustained Cure	All or most pretherapy signs and symptoms of the index infection have resolved (or returned to "preinfection status") with no evidence of resurgence AND no additional antibiotic therapy is/was required.
Failure	Patients carried forward with this status from the 5- to 9-day posttherapy EFU visit.
Relapse	Patients with a favorable clinical response (cure) at the 5- to 9-day posttherapy (EFU) visit have worsening signs and symptoms by the 28- to 42-day posttherapy (LFU) visit.
Indeterminate	Study data are not available for evaluation of efficacy for any reason, including: (a) Complication related to underlying medical condition (b) Patient was withdrawn for any reason before sufficient data had been obtained to permit evaluation of clinical response (c) Extenuating circumstances preclude classification as "cure," "relapse," or "failure" (d) Death occurred during the study period and the index infection was clearly noncontributory

APPENDIX 2. Assessment of Response

2. Global Response

At a fixed time-point occurring 28 (+7 days) post-randomization (GFU visit), a global response assessment was performed. The global response rating considered a variety of factors, including an assessment of signs and symptoms, all-cause mortality, requirement for unplanned surgical interventions, use of non-study antibiotics, and clinical instability/worsening during the course of the trial (Table 4). A favorable global response rating at the GFU visit was "cure." An unfavorable global response rating at the GFU visit was "failure." Patients with a global response rating of "indeterminate" at the GFU visit were counted as having an unfavorable global response for the GFU visit in the microbiological intention to treat (MITT) population.

Table 4
Definitions of Global Response at the GFU Visit

Global Response	Response Definition
Cure	Patient meets all 5 of the following criteria: (a) All pretherapy signs and symptoms of the baseline intraabdominal infection have resolved in the patient by the GFU visit; AND (b) The patient survived through the GFU visit; AND (c) The patient did **not** have an unplanned surgical procedure or percutaneous drainage procedure related to the baseline (or an emergent) intraabdominal infection at anytime through the GFU visit; AND (d) The patient did **not** receive any antibacterial drug therapy (e.g., rescue antibacterial drug therapy) to treat the baseline (or an emergent) intra-abdominal infection at any time after IV study therapy was initiated and through the GFU visit; AND (e) The patient did **not** suffer any other event related to the baseline (or an emergent) intra-abdominal infection which resulted in clinical instability or clinical worsening of the patient through the GFU visit.
Failure	Patient does not fulfill 1 or more of the 5 criteria outlined above for "cure"
Indeterminate	Study data are not available for evaluation of global response for any reasons at the GFU visit, including: (a) Complication related to underlying medical condition (b) Patient was withdrawn for any reason before sufficient data had been obtained to permit evaluation of global response (c) Extenuating circumstances preclude classification as "cure" or "failure"

APPENDIX 2. Assessment of Response

3. Microbiological Response

3.1. Assessment of Microbiological Response by Pathogen

Cultures of Site of Infection

Microbiological cultures (aerobic and anaerobic) were obtained from the IAI site of infection at baseline (previously obtained during the operative procedure) for all postsurgical patients and within 24 hours of study entry for all pre-surgical patients (during the operative procedure).

In addition, as clinically indicated and available, follow-up cultures from the site of infection were collected throughout the course of IV study therapy or the post-antibiotic follow-up period. In particular, follow-up cultures from the site of infection were to be obtained at the time of any surgical or drainage procedure. Follow-up cultures of the site of infection were also to be obtained, as clinically appropriate and medically appropriate, at any time there was clinical or laboratory evidence of persistence or progression of the infectious process (including persistent fever, elevated WBC count, or significant changes in the patient's clinical condition).

Culture results were tabulated according to organism, species, antibiotic susceptibility patterns, and microbiologic response. Patients with an appropriate clinical diagnosis from whom no etiologic bacterial pathogens were obtained were identified as "no pathogen isolated" and were excluded from the microbiological response assessments in the microbiologically evaluable population.

Blood Cultures

Patients with identified bacteremia (positive blood cultures) at admission were to have follow-up blood cultures and susceptibility testing collected daily until 2 consecutive cultures demonstrated no growth. Organisms isolated in the blood at admission were assigned a microbiologic response at each visit, similar to those given for IAI cultures (eradication, persistence, indeterminate). Organisms commonly considered to be blood culture contaminants were not included in evaluation of microbiologic response.

APPENDIX 2. Assessment of Response

3.2. Assessment of Overall Microbiological Response

The microbiological response was determined at completion of IV study therapy (DCIV), at the 5- to 9-day posttreatment (EFU) visit, the Day 28 (+7 day) post-randomization (GFU) visit, and the 28- to 42-day posttreatment (LFU) visit based on the results of available IAI cultures collected at any visit relative to the pathogen(s) isolated at baseline/admission.

At each time point subsequent to enrollment, a microbiological response was assessed separately for **each** pathogen identified in the admission culture. Microbiological response was based on the results of the culture and susceptibility testing of specimens obtained at any time a follow-up operative intervention was performed during IV study therapy or posttreatment follow-up. Favorable microbiological response assessments included "eradication" and "presumptive eradication." Unfavorable microbiological response assessments included "persistence" or "persistence acquiring resistance." For patients from whom only one pathogen was isolated, the overall microbiological response assessment was based on the microbiological response assessment for that pathogen. For patients in whom more than one baseline pathogen was isolated, the overall microbiological response assessment was "favorable" only if the microbiological response assessment for each of the baseline pathogens was "favorable."

To be considered a favorable microbiologic response, patients should preferably have had negative cultures ("eradication"). However, it was expected that in situations of clinical cure, no further invasive procedures would be performed and, therefore, the microbiological response was considered "presumptive eradication." A "presumptive eradication" was also a favorable microbiological response.

Patients with a microbiological response assessment of "indeterminate" were excluded from the microbiologically evaluable population for that assessment. If a patient was discontinued from IV study therapy due to clinical failure (and treated with non-study antibiotics), but persistence of the admission pathogen was not confirmed by culture results or no valid culture was obtained at the time of clinical failure, the admission pathogen was presumed to have persisted (i.e., "persistence").

Bacteria first encountered after the admission culture ("superinfection" if acquired during IV study therapy, or "new infection" if first isolated after the completion of IV study therapy) were evaluated separately.

Microbiological Response at the DCIV Visit

Microbiological responses at the DCIV visit were assessed as favorable ("eradication" or "presumptive eradication") or unfavorable ("persistence" or "persistence with acquisition of resistance") for each patient. This was assessed separately for each pathogen identified at admission. For a favorable overall microbiological assessment, all bacterial pathogens identified at baseline must have been eradicated or presumed eradicated, as appropriate, in follow-up cultures collected at/prior to the DCIV visit. In addition, the pathogen could not be present in follow-up blood cultures (if collected).

If a patient was discontinued from IV study therapy due to clinical failure (and treated with non-study antibiotics), but persistence of the admission pathogen was not confirmed by culture results or no valid culture was obtained at the time of clinical failure, the admission pathogen was presumed to have persisted (i.e., "persistence").

The criteria for the microbiologic response definitions at the DCIV visit are outlined in Table 5. Bacteria first encountered after the admission culture while on IV study therapy ("superinfection") were evaluated separately.

APPENDIX 2. Assessment of Response

Table 5
Definitions of Microbiologic Response at the DCIV Visit

Microbiological Response	Response Definition
Eradication	The follow-up culture at the site of infection taken at the DCIV visit (or, if not available, from the last available culture after at least 48 hours of IV study therapy) shows absence of all causative organisms.
Presumptive eradication	Absence of material to culture from the site of infection in a patient who had responded clinically to treatment.
Persistence	Any causative organism still present from culture taken at the DCIV visit (or from the last available culture after at least 48 hours of IV study therapy) from an intra-abdominal abscess, peritonitis, or surgical wound infection.
Persistence with acquisition of resistance	A culture at the site of infection taken at the DCIV visit (or from the last available culture after at least 48 hours of IV study therapy), grows a pathogen species that was previously susceptible to imipenem, but now has documented resistance to imipenem.
Superinfection	Emergence of a new pathogen from a culture taken at the DCIV visit (or the last available culture after at least 48 hours of IV study therapy), either at the site of infection or at a distant site, with emergence or worsening signs and symptoms of infection.
Indeterminate	Any of the following criteria are met: (a) Entry culture at the site of infection either not obtained or no growth (b) Follow-up cultures are not available from the site of infection due to patient death or withdrawal from study (c) Microbiological data are incomplete (d) Assessment not possible due to protocol violation (e) Any other circumstance which makes it impossible to define the microbiological response

Microbiologic Outcome at the EFU, GFU, and LFU Visits

Microbiologic response will also be determined at the EFU visit (5 to 9 days posttherapy), GFU visit (at Day 28 [+7 days] post-randomization), and at the LFU visit (28 to 42 days posttherapy).

For a favorable microbiological response, all bacterial pathogens identified at baseline must have been eradicated or presumed eradicated, as appropriate, in follow-up cultures collected at/prior to the respective follow-up visit. In addition, the pathogen could not be present in follow-up blood cultures (if collected).

The criteria for the microbiologic response definitions at the EFU, GFU, and LFU visits are outlined in Table 6. Bacteria first encountered after the admission culture and following the completion of IV study therapy ("new infection") were evaluated separately.

APPENDIX 2. Assessment of Response

Table 6
Definitions of Microbiologic Response at the EFU, GFU, and LFU Visits

Microbiological Response	Response Definition
Sustained eradication	A culture from the site of infection, taken at or up until the respective follow-up visit, shows continued absence of all causative organisms.
Persistence	Any causative organism still present at the end of IV study therapy (DCIV) from a culture of intra-abdominal abscess, peritonitis, or surgical wound infection. These patients are carried forward with this status from the DCIV visit to the 2 follow-up visits.
Persistence with acquisition of resistance	The culture from the site of infection at the end of IV study therapy (DCIV) grows any pathogen that was previously susceptible to imipenem, but now has documented resistance to imipenem. These patients are carried forward with this status from the DCIV visit to the 2 follow-up visits.
New infection	Eradication of the original pathogen from the site of infection followed by replacement (at the same site and after completion of IV study therapy) by a new species or by a new serotype or biotype of the same organism in the presence of signs or symptoms of infection. If a pathogen was isolated from a site distant to the primary infection after IV study therapy has been completed, then this is also designated as a new infection. A new infection identified at the EFU will be carried forward to the GFU and LFU visit. Similarly, a new infection identified at the GFU will be carried forward to the LFU visit.
Recurrence	A culture from the site of infection taken anytime after documented eradication at the DCIV visit grows the original pathogen. Recurrence identified at the EFU will be carried forward to the GFU and LFU visit. Similarly, recurrence identified at the GFU will be carried forward to the LFU visit.
Recurrence with acquisition of resistance	A culture from the site of infection taken anytime after documented eradication at the DCIV visit grows the original pathogen and has documented resistance to any study drug. Recurrence with acquisition of resistance identified at the EFU will be carried forward to the GFU and LFU visit. Similarly, recurrence with acquisition of resistance identified at the GFU will be carried forward to the LFU and LFU visit.
Indeterminate	Any of the following criteria are met: (a) Entry culture either not obtained or no growth (b) Follow-up cultures are not available due to patient death or withdrawal from study (c) Microbiological data are incomplete (d) Assessment not possible due to protocol violation (e) Any other circumstance which makes it impossible to define the microbiological response

APPENDIX 3. Subjects Excluded from Analysis (Randomized Population)

	REL 250 mg + IMI (N=118) n (%)	REL 125 mg + IMI (N=116) n (%)	Placebo + IMI (N=117) n (%)	Total (N=351) n (%)
MITT Evaluable				
Yes	89 (75.4)	96 (82.8)	92 (78.6)	277 (78.9)
No	29 (24.6)	20 (17.2)	25 (21.4)	74 (21.1)
Received less than one dose of IV study therapy	1 (0.8)	2 (1.7)	1 (0.9)	4 (1.1)
Baseline culture does not meet protocol-specified requirement	28 (23.7)	18 (15.5)	24 (20.5)	70 (19.9)
Microbiologically Evaluable				
Yes	83 (70.3)	87 (75.0)	85 (72.6)	255 (72.6)
No	35 (29.7)	29 (25.0)	32 (27.4)	96 (27.4)
Baseline culture does not meet protocol-specified requirement	28 (23.7)	18 (15.5)	24 (20.5)	70 (19.9)
Inadequate duration of IV study therapy	4 (3.4)	8 (6.9)	3 (2.6)	15 (4.3)
Prior or concomitant antimicrobials violation	2 (1.7)	2 (1.7)	2 (1.7)	6 (1.7)
Incorrect IV study therapy	1 (0.8)	0 (0.0)	2 (1.7)	3 (0.9)
Other	0 (0.0)	1 (0.9)	1 (0.9)	2 (0.6)
Study drug outside of stability	0 (0.0)	1 (0.9)	1 (0.9)	2 (0.6)
MITT = microbiological intention to treat.				

APPENDIX 4. Proportion of Subjects with Favorable Clinical Response at DCIV, by Baseline Pathogen (ME Population)

	Treatment Group						Comparison Between Treatment Groups †	
	REL 250 mg + IMI (N=81)		REL 125 mg + IMI (N=86)		Placebo + IMI (N=83)		REL 250 mg + IMI Vs Placebo + IMI	REL 125 mg + IMI Vs Placebo + IMI
	n/m	Response % (95 % CI)‡	n/m	Response % (95 % CI)‡	n/m	Response % (95 % CI)‡	Difference (95 % CI)	Difference (95 % CI)
Any Isolate	**76/79**	**96.2 (89.3, 99.2)**	**82/83**	**98.8 (93.5, 100.0)**	**77/81**	**95.1 (87.8, 98.6)**	**1.1 (-6.3, 8.8)**	**3.7 (-2.1, 11.0)**
Gram-Positive Aerobic Cocci	**32/32**	**100.0 (89.1, 100.0)**	**32/33**	**97.0 (84.2, 99.9)**	**33/34**	**97.1 (84.7, 99.9)**	**2.9 (-8.1, 15.1)**	**-0.1 (-12.9, 12.4)**
Enterococcus avium	2/2	100.0	3/3	100.0	4/4	100.0 (39.8, 100.0)	0.0	0.0
Enterococcus durans	1/1	100.0						
Enterococcus faecalis	7/7	100.0 (59.0, 100.0)	5/5	100.0 (47.8, 100.0)	5/5	100.0 (47.8, 100.0)	0.0 (-37.4, 45.6)	0.0 (-46.1, 46.1)
Enterococcus faecium	4/4	100.0 (39.8, 100.0)	4/4	100.0 (39.8, 100.0)	3/3	100.0	0.0	0.0
Enterococcus gallinarum			1/1	100.0	0/1	0.0		100.0
Enterococcus species					2/2	100.0		
Gemella morbillorum			1/1	100.0				
Lactococcus lactis	1/1	100.0						
Micrococcus luteus					1/1	100.0		
Staphylococcus aureus	6/6	100.0 (54.1, 100.0)	1/1	100.0	6/6	100.0 (54.1, 100.0)	0.0 (-41.1, 41.1)	0.0
Staphylococcus capitis			1/1	100.0				
Staphylococcus caprae	1/1	100.0						
Staphylococcus epidermidis	2/2	100.0	1/1	100.0	1/1	100.0	0.0	0.0
Staphylococcus haemolyticus			1/1	100.0				
Staphylococcus hominis	1/1	100.0						
Staphylococcus lugdunensis	1/1	100.0						
Streptococcus Group F	1/1	100.0						
Streptococcus agalactiae			1/1	100.0	1/1	100.0		0.0
Streptococcus anginosus	5/5	100.0 (47.8, 100.0)	6/6	100.0 (54.1, 100.0)	7/7	100.0 (59.0, 100.0)	0.0 (-45.6, 37.4)	0.0 (-41.0, 37.3)
Streptococcus anginosus group			1/1	100.0				
Streptococcus constellatus	2/2	100.0	5/6	83.3 (35.9, 99.6)	6/6	100.0 (54.1, 100.0)	0.0	-16.7 (-57.9, 28.5)
Streptococcus gallolyticus			2/2	100.0				
Streptococcus intermedius			1/1	100.0	1/1	100.0		0.0
Streptococcus mitis			1/1	100.0				
Streptococcus oralis			1/1	100.0				
Streptococcus salivarius	2/2	100.0			1/1	100.0	0.0	

APPENDIX 4 (cont.). Proportion of Subjects with Favorable Clinical Response at DCIV, by Baseline Pathogen (ME Population)

	Treatment Group						Comparison Between Treatment Groups †	
	REL 250 mg + IMI (N=81)		REL 125 mg + IMI (N=86)		Placebo + IMI (N=83)		REL 250 mg + IMI Vs Placebo + IMI	REL 125 mg + IMI Vs Placebo + IMI
	n/m	Response % (95 % CI)‡	n/m	Response % (95 % CI)‡	n/m	Response % (95 % CI)‡	Difference (95 % CI)	Difference (95 % CI)
Streptococcus sanguinis			1/1	100.0				
Streptococcus species	1/1	100.0	1/1	100.0				
Streptococcus viridans group			1/1	100.0	1/1	100.0		0.0
Gram-Positive Anaerobic Bacilli	**3/5**	**60.0 (14.7, 94.7)**	**6/6**	**100.0 (54.1, 100.0)**	**7/9**	**77.8 (40.0, 97.2)**	**-17.8 (-63.0, 29.9)**	**22.2 (-22.7, 55.8)**
Clostridium baratii			1/1	100.0				
Clostridium clostridioforme			2/2	100.0				
Clostridium perfringens	1/2	50.0	3/3	100.0	3/5	60.0 (14.7, 94.7)	-10.0	40.0
Clostridium ramosum			1/1	100.0				
Clostridium subterminale	1/1	100.0	1/1	100.0				
Eggerthella lenta	1/1	100.0			1/1	100.0	0.0	
Lactobacillus gasseri					1/1	100.0		
Lactobacillus species	0/1	0.0						
Propionibacterium acnes					2/2	100.0		
Gram-Positive Anaerobic Cocci	**1/1**	**100.0**	**3/3**	**100.0**	**4/4**	**100.0 (39.8, 100.0)**	**0.0**	**0.0**
Parvimonas micra	1/1	100.0	2/2	100.0	1/1	100.0	0.0	0.0
Peptoniphilus asaccharolyticus					1/1	100.0		
Peptostreptococcus anaerobius			1/1	100.0				
Peptostreptococcus prevotii					1/1	100.0		
Peptostreptococcus species					1/1	100.0		
Gram-Negative Aerobic Bacilli	**73/75**	**97.3 (90.7, 99.7)**	**73/73**	**100.0 (95.1, 100.0)**	**68/72**	**94.4 (86.4, 98.5)**	**2.9 (-4.4, 11.2)**	**5.6 (0.4, 13.5)**
Acinetobacter baumanii complex	2/2	100.0			3/3	100.0	0.0	
Acinetobacter lwoffii	1/1	100.0						
Alcaligenes xylosoxidans	2/2	100.0						
Citrobacter braakii					2/2	100.0		
Citrobacter freundii	1/1	100.0	2/2	100.0				
Citrobacter koseri					0/1	0.0		
Citrobacter youngae	1/1	100.0			1/1	100.0	0.0	
Comamonas kerstersii					1/1	100.0		

APPENDIX 4 (cont.). Proportion of Subjects with Favorable Clinical Response at DCIV, by Baseline Pathogen (ME Population)

	Treatment Group						Comparison Between Treatment Groups †	
	REL 250 mg + IMI (N=81)		REL 125 mg + IMI (N=86)		Placebo + IMI (N=83)		REL 250 mg + IMI Vs Placebo + IMI	REL 125 mg + IMI Vs Placebo + IMI
	n/m	Response % (95 % CI)‡	n/m	Response % (95 % CI)‡	n/m	Response % (95 % CI)‡	Difference (95 % CI)	Difference (95 % CI)
Comamonas testosteroni			1/1	100.0	1/1	100.0		0.0
Enterobacter aerogenes	2/2	100.0			1/1	100.0	0.0	
Enterobacter cloacae	7/7	100.0 (59.0, 100.0)	4/4	100.0 (39.8, 100.0)	4/4	100.0 (39.8, 100.0)	0.0 (-37.6, 51.4)	0.0 (-52.3, 52.3)
Enterobacter intermedius			1/1	100.0				
Escherichia coli	53/55	96.4 (87.5, 99.6)	56/56	100.0 (93.6, 100.0)	47/51	92.2 (81.1, 97.8)	4.2 (-5.7, 15.4)	7.8 (1.1, 18.6)
Escherichia fergusonii			1/1	100.0				
Hafnia alvei					2/2	100.0		
Klebsiella oxytoca	2/2	100.0	8/8	100.0 (63.1, 100.0)	2/3	66.7	33.3	33.3
Klebsiella pneumoniae	10/10	100.0 (69.2, 100.0)	12/12	100.0 (73.5, 100.0)	10/12	83.3 (51.6, 97.9)	16.7 (-14.4, 45.5)	16.7 (-10.6, 45.4)
Morganella morganii	2/2	100.0	1/1	100.0	2/2	100.0	0.0	0.0
Proteus mirabilis	8/8	100.0 (63.1, 100.0)	4/4	100.0 (39.8, 100.0)	6/6	100.0 (54.1, 100.0)	0.0 (-34.1, 40.8)	0.0 (-51.6, 41.6)
Proteus penneri			1/1	100.0				
Proteus vulgaris	1/1	100.0						
Pseudomonas aeruginosa	11/11	100.0 (71.5, 100.0)	13/13	100.0 (75.3, 100.0)	10/12	83.3 (51.6, 97.9)	16.7 (-12.4, 45.5)	16.7 (-9.0, 45.4)
Pseudomonas putida					1/1	100.0		
Raoultella planticola	1/1	100.0						
Salmonella species					1/1	100.0		
Serratia liquefaciens			1/1	100.0				
Serratia marcescens	1/1	100.0						
Stenotrophomonas maltophilia			3/3	100.0				
Gram-Negative Anaerobic Bacilli	**22/24**	**91.7 (73.0, 99.0)**	**30/30**	**100.0 (88.4, 100.0)**	**26/27**	**96.3 (81.0, 99.9)**	**-4.6 (-23.0, 11.4)**	**3.7 (-8.1, 18.5)**
Bacteroides caccae	2/2	100.0	1/1	100.0	1/1	100.0	0.0	0.0
Bacteroides distasonis	3/3	100.0	2/2	100.0	4/4	100.0 (39.8, 100.0)	0.0	0.0
Bacteroides eggerthii	1/1	100.0						
Bacteroides fragilis	11/11	100.0 (71.5, 100.0)	8/8	100.0 (63.1, 100.0)	12/12	100.0 (73.5, 100.0)	0.0 (-26.7, 25.1)	0.0 (-33.6, 25.2)
Bacteroides fragilis group			1/1	100.0				
Bacteroides ovatus	2/2	100.0	6/6	100.0 (54.1, 100.0)	4/4	100.0 (39.8, 100.0)	0.0	0.0 (-41.6, 51.6)
Bacteroides stercoris	2/2	100.0	1/1	100.0	2/2	100.0	0.0	0.0

APPENDIX 4 (cont.). Proportion of Subjects with Favorable Clinical Response at DCIV, by Baseline Pathogen (ME Population)

	Treatment Group						Comparison Between Treatment Groups †	
	REL 250 mg + IMI (N=81)		REL 125 mg + IMI (N=86)		Placebo + IMI (N=83)		REL 250 mg + IMI Vs Placebo + IMI	REL 125 mg + IMI Vs Placebo + IMI
	n/m	Response % (95 % CI)‡	n/m	Response % (95 % CI)‡	n/m	Response % (95 % CI)‡	Difference (95 % CI)	Difference (95 % CI)
Bacteroides thetaiotaomicron	6/6	100.0 (54.1, 100.0)	6/6	100.0 (54.1, 100.0)	6/7	85.7 (42.1, 99.6)	14.3 (-29.9, 52.8)	14.3 (-29.9, 52.8)
Bacteroides uniformis	1/1	100.0	8/8	100.0 (63.1, 100.0)	4/4	100.0 (39.8, 100.0)	0.0	0.0 (-34.4, 51.2)
Bacteroides vulgatus	2/4	50.0 (6.8, 93.2)	3/3	100.0	3/3	100.0	-50.0	0.0
Fusobacterium mortiferum	1/1	100.0						
Fusobacterium nucleatum	1/1	100.0	4/4	100.0 (39.8, 100.0)	1/1	100.0	0.0	0.0
Prevotella buccae			1/1	100.0				
Prevotella disiens	1/1	100.0						
Prevotella intermedia			1/1	100.0	3/3	100.0		0.0
Prevotella loescheii					1/1	100.0		
Prevotella melaninogenica	1/1	100.0	4/4	100.0 (39.8, 100.0)	1/1	100.0	0.0	0.0
Prevotella oralis			1/1	100.0				
Gram-Negative Anaerobic Cocci			**1/1**	**100.0**				
Veillonella dispar			1/1	100.0				
Gram-Negative Bacilli	**1/1**	**100.0**						
Non-lactose fermenting gram negative bacillus	1/1	100.0						

† 95% confidence intervals of between-treatment differences are based on unconditional asymptotic Miettinen and Nurminen method without stratification.

‡ 95% confidence intervals of response rate are based on the exact (Clopper-Pearson) method.

One patient may have more than one isolate and may be listed in this table more than once.

Subjects with indeterminate or missing response are excluded from the analysis.

N = Number of microbiologically evaluable subjects in each treatment group at DCIV.

n/m = Number of subjects with pathogen with favorable assessment/number of subjects with pathogen and assessment.

CI = Confidence interval. IPM/CIL = imipenem/cilastatin.