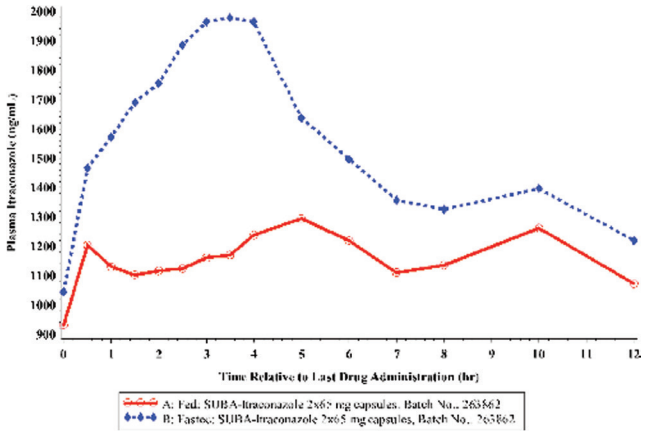
Figure 2: Mean plasma itraconazole concentration–time profile (day 15).



Disclosures. **J. Lindsay**, Mayne Pharma: Consultant, Consulting fee. **S. Mudge**, Mayne Pharma: Employee, Salary.

1355. Global Activity of Imipenem–Relebactam and Comparators Against Clinical Gram-Negative Pathogens – SMART 2017

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Background. Relebactam (REL), formerly MK-7655, is a β-lactamase inhibitor of class A and C β-lactamases that is in development in combination with imipenem (IMI). In this study, we evaluated the activity of IMI/REL against recent clinical isolates of Gram-negative bacilli (GNB) collected globally as part of the SMART surveillance program.

Methods. In 2017, 188 hospitals in 54 countries each collected up to 100 consecutive Gram-negative aerobic or facultatively anaerobic pathogens from lower respiratory tract infections, 75 from intra-abdominal infections, and 75 from urinary tract infections. MICs were determined for 41,319 GNB, including 30,864 *Enterobacteriaceae* and 6,933 *P. aeruginosa* isolates, using CLSI broth microdilution and interpreted with CLSI breakpoints; for comparison purposes, IMI susceptible breakpoints were applied to IMI/REL.

Results. Susceptibilities to IMI/REL and comparators of the 10 most commonly found *Enterobacteriaceae* species and *P. aeruginosa* are shown below.

Species	n	IMI/REL	IMI	FEP	CAZ	P/T	ATM	CIP	AMK	CST
E. coli	14176	99.5	99.0	75.8	79.0	91.0	76.1	64.4	99.0	99.6
K. pneumoniae	7208	92.5	86.9	59.0	58.2	68.6	58.5	60.4	93.8	95.1
P. mirabilis	1670	63.1	63.6	88.3	90.7	97.5	94.3	65.9	96.1	0.4
E. cloacae	1601	96.7	93.7	75.3	62.2	72.1	63.2	81.8	97.7	93.1
S. marcescens	1129	70.2	51.6	91.1	91.6	92.2	90.0	89.6	98.1	5.2
K. oxytoca	1012	99.2	98.5	94.3	93.9	86.8	86.9	94.1	99.5	99.2
K. aerogenes	828	97.5	88.3	92.6	72.1	75.0	75.4	93.8	98.9	98.6
C. freundii	568	98.6	96.7	90.7	70.8	79.6	71.8	87.0	99.1	99.8
M. morganii	538	32.0	5.6	94.4	84.4	97.4	94.1	76.8	99.3	0.6
C. koseri	402	98.5	96.0	98.3	97.8	97.3	96.5	98.5	99.8	100
P. aeruginosa	6933	88.8	68.6	74.6	73.4	68.3	63.9	74.8	90.7	99.5

IMI, imipenem, REL, relebactam, FEP, cefepime; CAZ, ceftazidime; P/T, piperacillin-tazobactam; ATM, aztreonam; AMK, amikacin; CIP, ciprofloxacin; CST, colistin; NA, breakpoint not available

IMI/REL showed activity >90% against seven of the top 10 *Enterobacteriaceae* species, typically ~5 to 35 percentage points higher than the β-lactam comparators, and it was active against 89% of *P. aeruginosa*, ~15 to 25 percentage points higher than the β-lactam comparators. Only amikacin and colistin showed similar or higher activity for most species, with colistin showing little activity against Proteeae and *Serratia*.

Conclusion. IMI/REL could provide an important treatment option against infections with Gram-negative pathogens, especially since amikacin and colistin are associated with significant morbidity, including nephrotoxicity and ototoxicity, and amikacin is typically used in combination with another antibiotic.

Disclosures. **S. Lob**, IHMA, Inc.: Employee, Salary. Merck: Consultant, Consulting fee. **K. Kazmierczak**, Merck: Consultant, Consulting fee. IHMA, Inc.: Employee, Salary. **D. Hoban**, IHMA, Inc.: Employee, Salary. Merck: Consultant, Consulting fee. **M. Hackel**, IHMA, Inc.: Employee, Salary. Merck: Consultant, Consulting fee. **K. Young**, Merck: Employee and Shareholder, Dividends and Salary. **M. Motyl**, Merck: Employee and Shareholder, Dividends and Salary. **D. Sahm**, IHMA, Inc.: Employee, Salary. Merck: Consultant, Consulting fee.

1356. Improvement in Quality of Life for Adults With Acute Bacterial Skin and Skin Structure Infections Following Treatment With Omadacycline or Linezolid

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Background. The appearance of multidrug-resistant Gram-positive bacteria is a major challenge in clinical care. Omadacycline is the first aminomethylcycline antibiotic (semisynthetic compounds related to tetracyclines) in late-stage clinical development for acute bacterial skin and skin structure infections (ABSSSI), and demonstrates potent *in vitro* activity against many pathogens.

Methods. Seven hundred thirty-five patients were enrolled in the OASIS-2 randomized controlled trial comparing omadacycline and linezolid for the treatment of adult subjects with ABSSSI known or suspected to be due to a Gram-positive pathogen, with 368 and 367 enrolled in each group, respectively. Subjects completed the 36-Item Short Form Health Survey Version 2 (SF-36v2), a validated questionnaire on physical and mental health, at both screening and post-treatment evaluation. Results of the SF-36v2 were analyzed in accordance with established norm-based standards for the survey (Ware 2000) for the intention-to-treat population.

Results. Subjects who received omadacycline experienced a 3.25 point mean improvement in overall physical health ($P < 0.001$, Figure 1) and reported significant improvements across all but one component parameter of overall physical and mental health, including physical functioning, bodily pain, role physical, vitality, role emotional, mental health, and social functioning (Figure 2). In contrast, while overall physical health improved for subjects who received linezolid, the improvement in vitality, role emotional, mental health, and general health was not significant (Figure 2). Although omadacycline achieved greater increase from baseline than linezolid across all domains analyzed, the difference in scores was not statistically significant at the $P < 0.05$ level (Figure 1).

Conclusion. Omadacycline provides significant improvement in the physical component of quality of life over baseline for adult subjects with ABSSSI known or suspected to be due to a Gram-positive pathogen. Although the OASIS-2 trial was neither designed nor powered to measure differences in quality of life following treatment, trends identified in this analysis merit further investigation.

References

1. Ware JE. SF-36 Health Survey Update. SPINE 2000; 25(24); 3130–3139.

Figure 1.

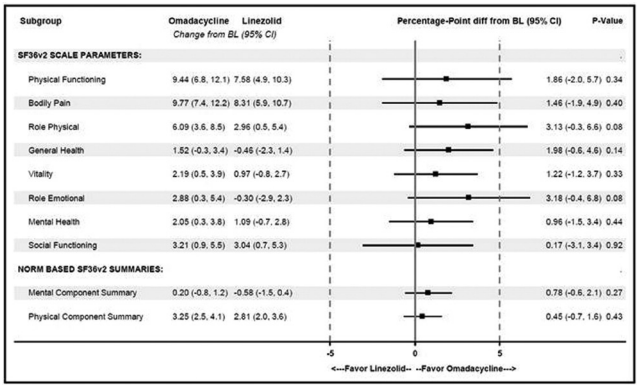
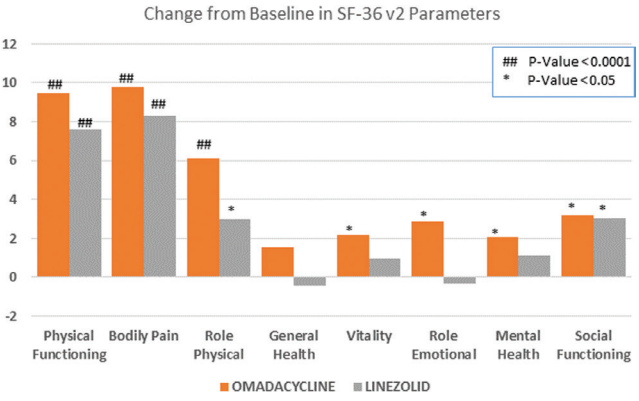


Figure 2.



Disclosures. **E. Tzanis**, Paratek Pharmaceuticals: Employee, Salary. **M. Curran**, Paratek Pharmaceuticals: Employee, Salary. **P. McGovern**, Paratek Pharmaceuticals: Employee, Salary. **J. Hinahara**, Paratek Pharmaceuticals: Consultant, Consulting fee. **T. Goss**, Paratek Pharmaceuticals: Consultant, Consulting fee.

1357. A Combination of Itraconazole and Amiodarone Is Highly Effective Against *Trypanosoma cruzi* Infection of Human Stem Cell-Derived Cardiomyocytes

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