qPCR supported both new acquisition of these genes and expansion of existing AMR pools. Further statistical analyses demonstrated significant correlations between changes in the gut resistome and clinical study parameters including β-lactamase gene frequency and study drug assignment, and efflux pump gene frequency and vancomycin resistance.

Conclusion. Taken together, these findings demonstrated that coadministration of ribaxamase with IV β-lactam antibiotics can protect the integrity of the gut microbiome and may help limit the emergence of AMR induced by these antibiotics.

Disclosures. **J. Kokai-Kun**, Synthetic Biologics, Inc.: Employee, Salary. **C. Le**, Synthetic Biologics, Inc.: Employee, Salary. **K. Trout**, Synthetic Biologics, Inc.: Employee, Salary. **J. Sliman**, Synthetic Biologics, Inc.: Employee, Salary.

1338. A Pooled Analysis of Patients With Wound Infections in the Phase 3 REVIVE Trials: Randomized, Double-blind Studies to EValuate the Safety and Efficacy of Iclaprim Vs. Vancomycin for trEatment of Acute Bacterial Skin and Skin Structure Infections

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Background. The objective of this evaluation was to provide an analysis of pooled efficacy data from two parallel Phase 3 trials of iclaprim, a diaminopyrimidine dihydrofolate reducatase inhibitor, compared with vancomycin for the treatment of patients with wound infections including surgical site infections (SSI).

Methods. A pooled analysis of patients with wound infections was conducted from two parallel Phase 3, double-blind, randomized (1:1), active-controlled, multinational, multicenter trials (REVIVE-1 and REVIVE-2), which included a total of 602 patients with wound infections. The data were analyzed separately and then pooled to determine the efficacy of iclaprim 80 mg fixed dose compared with vancomycin 15 mg/kg. Both drugs were administered intravenously every 12 hours for 5 to 14 days according to the investigator assessment of clinical response. The primary endpoint of these studies was to determine whether iclaprim was noninferior (NI; 10% margin) to vancomycin in achieving a ≥20% reduction in lesion size (early clinical response [ECR] at 48 to 72 hours after initiation of the study drug (early time point [ETP]), compared with baseline in the intent-to-treat (ITT) population.

Results. Iclaprim had similar ECR rates at ETP compared with vancomycin among the subset of patients with wound infections (see table). The median treatment duration for both iclaprim and vancomycin was 7 days (range 5–14 days).

	REVIVE-1		REVIVE-2		Combined REVIVE-1/2	
	Iclaprim (*N* = 182)	Vancomycin (*N* = 158)	Iclaprim (*N* = 127)	Vancomycin (*N* = 135)	Iclaprim (*N* = 309)	Vancomycin (*N* = 293)
Early Clinical Response, *n* (%)	152 (83.5)	126 (79.7)	105 (82.7)	103 (76.3)	257 (83.2)	229 (78.2)
% Difference (iclaprim–vancomycin)	3.77		6.38		5.01	
95% CI	–4.50, 12.04		–3.35, 16.12		–1.29, 11.32	

Conclusion. In this post-hoc analysis of the REVIVE studies, iclaprim achieved NI to vancomycin in both studies, based on ECR at ETP, in the subgroup of patients with wound infections. These results suggest that iclaprim may be a valuable treatment option for patients with wound infections, including SSI, suspected or confirmed to be due to Gram-positive pathogens.

Disclosures. **D. Huang**, Motif BioSciences: Employee, Salary. **G. R. Corey**, Motif BioSciences: Board Member, Consulting fee. **T. L. Holland**, Basilea: Consultant, Consulting fee. Motif Bio: Consultant and Scientific Advisor, Consulting fee. Theravance: Consultant, Speaker honorarium. Genentech: Consultant, Consulting fee. **T. P. Lodise Jr.**, Motif BioSciences: Board Member, Consulting fee. **W. O'Rirodan**, Motif BioSciences: Board Member, Consulting fee. **M. Wilcox**, Motif BioSciences: Board Member, Consulting fee. **T. M. File Jr.**, Motif BioSciences: Board Member, Consulting fee. **M. Dryden**, Motif BioSciences: Board Member, Consulting fee. **B. Balser**, Motif BioSciences: Consultant, Consulting fee. **E. Desplats**, Motif BioSciences: Consultant, Consulting fee.

1339. Results for the Supplemental Microbiological Modified Intent-to-Treat (SmMITT) Population of the RESTORE-IMI 1 Trial of Imipenem/Cilastatin/Relebactam (IMI/REL) vs. Imipenem/Cilastatin Plus Colistin (IMI+CST) in Patients with Imipenem-Nonsusceptible (NS) Bacterial Infections

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Background. Clinical trials of new antibacterial agents in patients with carbapenem-resistant infections are critical but challenging to conduct. One challenge is identifying the study population by microbiological (micro) criteria; patients need to be identified locally to initiate effective treatment rapidly, but data standardization requires central laboratory confirmation. REL is a novel β-lactamase inhibitor that can restore imipenem activity against many imipenem-NS Gram-negative pathogens. Here we compare a supplemental analysis population based on local microbiology data (SmMITT eligibility) with the primary analysis population (mMITT) from the RESTORE-IMI 1 trial (NCT02452047) of IMI/REL vs. IMI+CST.

Methods. Randomized, active-controlled, double-blind, phase 3 trial enrolled adults with hospital-acquired/ventilator-associated bacterial pneumonia (HABP/VABP), complicated intra-abdominal infection (cIAI), or complicated urinary tract infection (cUTI). Patients were mMITT-eligible if pathogens were imipenem-NS (but CST- and IMI/REL-susceptible) based on central laboratory minimum inhibitory concentration (MIC). SmMITT comprised mMITT plus all patients who met inclusion criteria only based on local laboratory MIC.

Results. The SmMITT population (n = 41 [28 IMI/REL; 13 IMI+CST]) comprised 31 from mMITT plus 10 based on local MIC; 12/41 (29%) had HABP/VABP, 8/41 (20%) cIAI, and 21/41 (51%) cUTI. The majority of differences in central vs. local MIC were 1–2 dilutions; similar numbers of patients were excluded from mMITT due to imipenem susceptibility (n = 5) or IMI/REL-NS (n = 4); 1 patient was CST-NS. Baseline characteristics, including infecting pathogens, were comparable in SmMITT and mMITT (SmMITT: 68% male; 46% ≥65 y; 24% APACHE II score >15; 22% creatinine clearance <60 mL/minute). Rates of efficacy outcomes (overall response, day 28 clinical response, day 28 mortality) were comparable between populations, except that response rates in patients with cIAI were higher in SmMITT (table).

Conclusion. Consistency of results was demonstrated across two analysis populations in a trial of resistant pathogens. This analysis provides results supportive of expected future clinical use of IMI/REL when treatment decisions will be made based on local laboratory results.

Table. Efficacy outcomes in pts in the mMITT and SmMITT populations

	IMI/REL[a]	IMI+CST[b]	Unadjusted Difference	Adjusted Difference
	n/m (%)	n/m (%)	% (90% CI)	% (90% CI)[c]
Favorable Overall Response[d]				
mMITT	15/21 (71.4)	7/10 (70.0)	1.4	-7.3 (-27.5, 21.4)
HABP/VABP cIAI cUTI	7/8 (87.5) 0/2 (0.0) 8/11 (72.7)	2/3 (66.7) 0/2 (0.0) 5/5 (100.0)	20.8 0.0 -27.3 (-52.8, 12.8)[e]	-
SmMITT	21/28 (75.0)	10/13 (76.9)	-1.9	-4.5 (-24.2, 20.7)
HABP/VABP cIAI cUTI	7/8 (87.5) 2/5 (40.0) 12/15 (80.0)	3/4 (75.0) 1/3 (33.3) 6/6 (100.0)	12.5 (-25.4, 56.6)[e] 6.7 -20.0 (-41.4, 14.2)[e]	-
Favorable Clinical Response (Day 28)				
mMITT	15/21 (71.4)	4/10 (40.0)	31.4	26.3 (1.3, 51.5)
SmMITT	21/28 (75.0)	7/13 (53.8)	21.2	17.6 (-5.9, 42.5)
All-Cause Mortality (Through Day 28)				
mMITT	2/21 (9.5)	3/10 (30.0)	-20.5	-17.3 (-46.4, 6.7)
SmMITT	3/28 (10.7)	3/13 (23.1)	-12.4	-10.5 (-35.2, 9.6)

[a]IMI/REL (500 mg imipenem/cilastatin and 250 mg relebactam) every 6 hours. [b]CST provided as colistimethate sodium (loading dose of 300 mg colistin base activity [CBA] followed by 150 mg CBA [corresponding to ≈360 mg colistimethate sodium or ≈4.5 million IU] every 12 hours). Imipenem/cilastatin (500 mg every 6 hours). [c]Adjusted differences and 90% CIs are based on Miettinen & Nurminen method stratified by infection-site stratum. [d]Overall response: (a) survival status through day 28 postrandomization in pts with HABP/VABP, (b) clinical response at day 28 postrandomization for pts with cIAI, and (c) the composite clinical and microbiological response at early follow-up for pts with cUTI. [e]90% CIs are based on Miettinen & Nurminen method.
n/m, number of pts with a favorable response or all-cause mortality/number of evaluable pts.

Disclosures. **K. Kaye**, Merck & Co., Inc.: Consultant and Research Contractor, Research grant. Melinta, Achaogen, Allergan: Consultant, Consulting fee. **T. File**, Bio Merieux, Curetis, Melinta, Merck, MotifBio, Nabriva, Paratek, Pfizer: Consultant, Consulting fee. **H. W. Boucher**, Merck & Co., Inc.: Scientific Advisor, Consulting fee. **M. Brown**, Merck & Co., Inc.: Employee, Salary. **A. Aggrey**, Merck & Co., Inc.: Employee, Salary. **I. Khan**, Merck & Co., Inc.: Employee, Salary. **H. K. Joeng**, Merck & Co., Inc.: Employee, Salary. **R. Tipping**, Merck & Co., Inc.: Employee, Salary. **J. Du**, Merck & Co., Inc.: Employee, Salary. **K. Young**, Merck & Co., Inc.: Employee, Salary and Stock options. **J. Butterton**, Merck & Co., Inc.: Employee, Salary and Stock. **N. A. Kartsonis**, Merck & Co., Inc.: Employee, Salary and Stocks. **A. Paschke**, Merck & Co., Inc.: Employee and Shareholder, Salary.

1340. Population Pharmacokinetic (PK) Analysis of APX001 Using Phase 1 Data

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Background. APX001 is a novel antifungal agent which is rapidly converted to the active metabolite APX001A. APX001A exhibits *in vitro* activity against many clinically important yeast and fungi, including echinocandin- and azole-resistant *Candida* species. Given this activity, intravenous (IV) and oral (PO) formulations of APX001 are being developed for