

alone were provisionally applied to FTB and MVB, respectively. Tazobactam, avibactam, and taniboractam were fixed at 4 µg/mL, while vaboractam was fixed at 8 µg/mL. Breakpoints from CLSI M100, 31st ed, 2021.

	AMK	ATM	C/T	CAZ	CZA	FEP	FTB	IPM	MEM	MVB	TZP	TOB
CLSI												
Susceptible	≤16	≤8	≤4/4	≤8	≤8/4	≤8	*	≤2	≤2	*	≤16/4	≤4
Breakpoint												
MIC₅₀	4	>16	4	>16	8	>16	8	>4	>4	>4	>64	1
MIC₉₀	>32	>16	>8	>16	>8	>16	>8	>4	>4	>4	>64	>8
%S	76.8	25.0	59.3	30.5	63.0	40.7	68.5	0.0	19.4	21.3	23.0	61.0

MIC₅₀ and MIC₉₀ values (µg/mL) and percent susceptibility (%S) for the subset of carbapenem-non-susceptible *P. aeruginosa* strains (n=108). AMK, amikacin; ATM, aztreonam; C/T, ceftiozane-tazobactam; CAZ, ceftazidime; CZA, ceftazidime-avibactam; FEP, cefepime; FTB, cefepime-taniboractam; IPM, imipenem; MEM, meropenem; MVB, meropenem-vaboractam; TZP, piperacillin-tazobactam; TOB, tobramycin. *The breakpoints for FEP and MEM alone were provisionally applied to FTB and MVB, respectively. Tazobactam, avibactam, and taniboractam were fixed at 4 µg/mL, while vaboractam was fixed at 8 µg/mL. Breakpoints from CLSI M100, 31st ed, 2021.

MIC50 and MIC90 values (µg/mL) and percent susceptibility (%S) for the subset of carbapenem-non-susceptible *P. aeruginosa* strains (n=108). AMK, amikacin; ATM, aztreonam; C/T, ceftiozane-tazobactam; CAZ, ceftazidime; CZA, ceftazidime-avibactam; FEP, cefepime; FTB, cefepime-taniboractam; IPM, imipenem; MEM, meropenem; MVB, meropenem-vaboractam; TZP, piperacillin-tazobactam; TOB, tobramycin. *The breakpoints for FEP and MEM alone were provisionally applied to FTB and MVB, respectively. Tazobactam, avibactam, and taniboractam were fixed at 4 µg/mL, while vaboractam was fixed at 8 µg/mL. Breakpoints from CLSI M100, 31st ed, 2021.

Conclusion. Compared to MVB, CZA, and C/T, FTB demonstrated the greatest activity against the 197 *P. aeruginosa* strains tested, including many carbapenem-non-susceptible strains. Pending completion of clinical development, FTB may be a promising therapeutic option for MDR *P. aeruginosa* infections.

Disclosures. Robin Patel, MD, 1928 Diagnostics (Consultant)BioFire Diagnostics (Grant/Research Support)ContraFect Corporation (Grant/Research Support)Curetis (Consultant)Hylomorph AG (Grant/Research Support)IDSA (Other Financial or Material Support, Editor's Stipend)Infectious Diseases Board Review Course (Other Financial or Material Support, Honoraria)Mammoth Biosciences (Consultant)NBME (Other Financial or Material Support, Honoraria)Netflix (Consultant)Next Gen Diagnostics (Consultant)PathoQuest (Consultant)PhAST (Consultant)Qvella (Consultant)Samsung (Other Financial or Material Support, Patent Royalties)Selux Diagnostics (Consultant)Shionogi & Co., Ltd. (Grant/Research Support)Specific Technologies (Consultant)TenNor Therapeutics Limited (Grant/Research Support)Torus Biosystems (Consultant)Up-to-Date (Other Financial or Material Support, Honoraria) Robin Patel, MD, BioFire (Individual(s) Involved: Self; Grant/Research Support; Contrafect (Individual(s) Involved: Self); Grant/Research Support; IDSA (Individual(s) Involved: Self); Editor's stipend; NBME, Up-to-Date and the Infectious Diseases Board Review Course (Individual(s) Involved: Self); Honoraria; Netflix (Individual(s) Involved: Self); Consultant; TenNor Therapeutics Limited (Individual(s) Involved: Self); Grant/Research Support; to Curetis, Specific Technologies, Next Gen Diagnostics, PathoQuest, Selux Diagnostics, 1928 Diagnostics, PhAST, Torus Biosystems, Mammoth Biosciences and Qvella (Individual(s) Involved: Self); Consultant David van Duin, MD, PhD, Entasis (Advisor or Review Panel member)genentech (Advisor or Review Panel member)Karius (Advisor or Review Panel member)Merck (Grant/Research Support, Advisor or Review Panel member)Pfizer (Consultant, Advisor or Review Panel member)Qpex (Advisor or Review Panel member)Shionogi (Grant/Research Support, Scientific Research Study Investigator, Advisor or Review Panel member)Utility (Advisor or Review Panel member) Vance G. Fowler, Jr., MD, MHS, Achaogen (Consultant)Advanced Liquid Logics (Grant/Research Support)Affinergy (Consultant, Grant/Research Support)Affinium (Consultant)Akagera (Consultant)Allergan (Grant/Research Support)Amphliph Biosciences (Consultant)Aridis (Consultant)Armata (Consultant)Basilea (Consultant, Grant/Research Support)Bayer (Consultant)C3J (Consultant)Cerexa (Consultant, Other Financial or Material Support, Educational fees)Contrafect (Consultant, Grant/Research Support)Debiopharm (Consultant, Other Financial or Material Support, Educational fees)Destiny (Consultant)Durata (Consultant, Other Financial or Material Support, educational fees)Genentech (Consultant, Grant/Research Support)Green Cross (Other Financial or Material Support, Educational fees)Integrated Biotherapeutics (Consultant)Janssen (Consultant, Grant/Research Support)Karius (Grant/Research Support)Locus (Grant/Research Support)Medical Biosurfaces (Grant/Research Support)Medicines Co. (Consultant)MedImmune (Consultant, Grant/Research Support)Merck (Grant/Research Support)NIH (Grant/Research Support)Novadigm (Consultant)Novartis (Consultant, Grant/Research Support)Pfizer (Grant/Research Support)Regeneron (Consultant, Grant/Research Support)sepsis diagnostics (Other Financial or Material Support, Pending patent for host gene expression signature diagnostic for sepsis.)Tetraphase (Consultant)Theravance (Consultant, Grant/Research Support, Other Financial or Material Support, Educational fees)Trius (Consultant)UpToDate (Other Financial or Material Support, Royalties)Valanbio (Consultant, Other Financial or Material Support, Stock options)xBiotech (Consultant) Daniel D. Rhoads, MD, Becton, Dickinson and Company (Grant/Research Support) Michael Jacobs, MBBS, Venatorx Pharmaceuticals, Inc. (Grant/Research Support) Focco van den Akker, PhD, Venatorx Pharmaceuticals, Inc. (Grant/Research Support) David A. Six, PhD, Venatorx Pharmaceuticals, Inc. (Employee) Greg Moeck, PhD, Venatorx Pharmaceuticals, Inc. (Employee) Krisztina M. Papp-Wallace, Ph.D., Merck & Co., Inc. (Grant/Research Support)Spero Therapeutics, Inc. (Grant/Research Support)Venatorx Pharmaceuticals, Inc. (Grant/Research Support)Wockhard Ltd. (Other Financial or Material Support, Research Collaborator) Robert A. Bonomo,

MD, entasis (Research Grant or Support)Merck (Grant/Research Support)NIH (Grant/Research Support)VA Merit Award (Grant/Research Support)VenatoRx (Grant/Research Support)

1064. Treatment Success in Reducing Recurrent *Clostridioides difficile* Infection with Investigational Live Biotherapeutic RBX2660 Is Associated with Microbiota Restoration: Consistent Evidence from a Phase 3 Clinical Trial

Ken Blount, PhD¹; Dana M. Walsh, PhD¹; Carlos Gonzalez, MS²; Bill Shannon, PhD MBA²; ¹Rebiotix, Inc., Roseville, Minnesota; ²BioRankings, LLC, St. Louis, Missouri

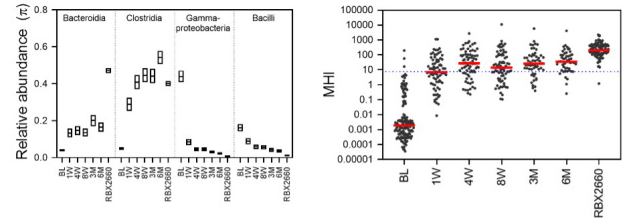
Session: P-61. Novel Agents

Background. Several investigational microbiota-based live biotherapeutics are in clinical development for reducing recurrence of *Clostridioides difficile* infection (rCDI), including RBX2660 a liquid suspension of a broad consortium of microbiota, which includes Bacteroidetes and Firmicutes. RBX2660 has been evaluated in >600 participants in 6 clinical trials. Here we report that RBX2660 induced significant shifts to the intestinal microbiota of treatment-responsive participants in PUNCH CD3—a Phase 3 randomized, double-blinded, placebo-controlled trial.

Methods. PUNCH CD3 participants received a single dose of RBX2660 or placebo between 24 to 72 hours after completing rCDI antibiotic treatment. Clinical response was the absence of CDI recurrence at eight weeks after treatment. Participants voluntarily submitted stool samples prior to blinded study treatment (baseline), 1, 4 and 8 weeks, 3 and 6 months after receiving study treatment. Samples were extracted and sequenced using shallow shotgun methods. Operational taxonomic unit (OTU) data were used to calculate relative taxonomic abundance, alpha diversity, and the Microbiome Health Index (MHI)—a biomarker of antibiotic-induced dysbiosis and restoration.

Results. Clinically, RBX2660 demonstrated superior efficacy versus placebo (70.4% versus 58.1%). From before to after treatment, RBX2660-treated clinical responders' microbiome diversity shifted significantly (Mann-Whitney), and so did microbiome composition (Generalized Wald Test). Post-treatment changes were characterized by increased Bacteroidia and Clostridia and decreased Gammaproteobacteria and Bacilli, changes and were durable to at least 6 months. Repeated measures analysis confirmed that shifts were greater among RBX2660 responders compared to placebo responders (DMRepeat). The majority of responders' MHI values shifted from a range common to antibiotic dysbiosis to a range common in healthy populations.

Figure 1



Left panel. Mean relative abundance taxonomic class level at timepoints for participants in PUNCH CD3 before and after RBX2660 treatment, and for doses of RBX2660 administered in PUNCH CD3. The four taxonomic classes that change most from before to after treatment are shown with the mean and confidence intervals based on fitting OTU data to a Dirichlet multinomial distribution. Right panel, MHI biomarker for the same time points and investigational product groups, shown as median (red) and individual samples. A previously calculated threshold of MHI = 7.2 is shown (dotted line), above which MHI values predict healthy, below which MHI values predict antibiotic-induced dysbiosis.

Conclusion. Among PUNCH CD3 clinical responders, RBX2660 significantly restored microbiota from less to more healthy compositions, and this restoration was durable to at least 6 months. These clinically-correlated microbiome shifts are highly consistent with results from multiple prior trials of RBX2660.

Disclosures. Ken Blount, PhD, Rebiotix Inc., a Ferring Company (Employee) Dana M. Walsh, PhD, Rebiotix (Employee)

1065. Efficacy of Cefiderocol in Experimental *Stenotrophomonas maltophilia* Pneumonia in Persistently Neutropenic Rabbits

Vidmantas Petraitis, MD¹; Ruta Petraitiene, MD¹; Povilas Kavaliauskas, MSc¹; Ethan Naing, MD²; Andrew Garcia, MS¹; Naoki Ishibashi, MD³; Benjamin Georgiades, n/a⁴; Roger Echols, MD⁵; Robert A. Bonomo, MD⁶; Yoshinori Yamano, PhD⁷; Thomas J. Walsh, MD, PhD (hon)⁸; ¹Weill Cornell Medicine of Cornell University, New York, NY; ²Transplantation-Oncology Infectious Disease Program, Translational Research Laboratory, Division of Infectious Diseases, Weill Cornell Medicine, New York, NY 10065, US, New York, NY; ³Pharmaceutical Research Division, Osaka, Osaka, Japan; ⁴Shionogi, Inc., Florham Park, New Jersey; ⁵Infectious Disease Drug Development Consulting LLC, Easton, Connecticut; ⁶Louis Stokes Cleveland VA Medical Center, Cleveland, OH; ⁷Shionogi & Co., Ltd., Osaka, Osaka, Japan; ⁸Weill Cornell Medicine, New York, NY

Session: P-61. Novel Agents

Background. *Stenotrophomonas maltophilia* causes lethal pneumonia, bacteremia, and sepsis in immunocompromised patients. As a standard of care,