LB3. Exebacase (EXE) Reduced Length of Stay and 30-Day Readmission Rates for US Patients with Methicillin-Resistant Staphylococcus aureus (MRSA) Bacteremia Including Endocarditis Compared with Standard of Care Antibiotics (SoC) Alone in a Phase 2 Study

Cara Cassino, MD; Cara Cassino, MD; Hemal Shah, PharmD; Joy Lipka-Diamond, MS; Anita F. Das, PhD; ContraFect Corporation, Yonkers, New York; Value Matters, Ridgefield, Connecticut; Lipka Consulting, Mullica Hill, New Jersey; AD Stat Consulting, Guerneville, California

Session: 83. Late Breaker Oral Abstract Session 1
Thursday, October 3, 2019: 2:05 PM

Background. Exebacase, a lysin (cell wall hydrolase), is the first direct lytic agent to report Phase 2 study results in Staphylococcus aureus bacteremia including endocarditis (ACM). Ninety-one patients were enrolled in their randomized, double-blind, placebo controlled study; EXE used in addition to standard of care antibiotics (SoC); had 42.8% higher clinical responder rates (CRRs) compared SoC alone. We sought to determine whether these differences in CRRs translated into reductions in health resource utilization (HRU) in this population of critically ill, hospitalized patients.

Methods. The microbiological intent-to-treat population included 116 patients (71 EXE, 45 SoC) with documented S. aureus who received a single 2-hour infusion of blinded study drug based on target attainment. The primary efficacy endpoint was CRR at Day 14. Diagnoses and clinical outcomes were determined by a blinded Adjudication Committee (HRR) including length of stay (LOS), and 30-day hospital readmission rates (HRR) for all causes (AC) and for S. aureus (SA) were evaluated in MRSA patients who were alive at the time of discharge.

Results. The average patient was white, male and ~56 years old (67.8%). Twenty-seven EXE patients (38.0%) and 16 SoC patients (35.6%) had MRSA. All but 2 MRSA patients (1 EXE, 1 SoC) were enrolled in the United States. The Day 14 CRR were 70.4% for EXE and 60.0% for SoC groups (p=0.314). Among a prespecified analysis of MRSA patients, the CRR with EXE was 74.1% vs. 31.3% with SoC (p = 0.010). Among patients who received study drug, incidence of treatment emergent adverse events (TEAEs) was balanced between groups (24 (88.9%) in EXE and 15 (98.3%) in SoC) as were serious TEAEs (17 (63.0%) in EXE, 12 (75%) in SoC). 1 EXE and 2 SoC US MRSA patients died in hospital. Among US MRSA patients discharged alive from the hospital, the median LOS after study drug was 6 vs. 10 days for EXE and SoC, respectively. Thirty-day AC HRR were 16% vs. 30.8%, for EXE vs. SoC, respectively, and 30-day SA HRR were 8% vs. 15.4%, respectively.

Conclusions. Exebacase used in addition to SoC was associated with a reduction in length of hospital stay and 30-day readmission rates for all causes and for S. aureus compared with SoC alone in patients being treated for MRSA bacteremia/endocarditis.

Disclosures. Cara Cassino, MD, ContraFect Corporation (Employee), Hemal Shah, PharmD, Boehringer Ingelheim (Consultant), ContraFect Corp (Consultant), DBV Technologies (Consultant), Mylan specialty (Consultant), NaBrava (Consultant), Joy Lipka-Diamond, MS, ContraFect Corporation (Consultant), Anita F. Das, PhD, Achaogen (Consultant), AntibioiTx (Consultant), Boston Pharmaceuticals (Consultant), Cempra (Consultant), ContraFect Corporation (Consultant), Iterum Therapeutics (Consultant), NaBrava (Consultant), Paratek (Consultant), Tetraphase (Consultant), UTILITY (Consultant), Wockhardt (Consultant).

LB4. Efficacy and Safety of Cefiderocol vs. High-Dose Meropenem in Patients with Nosocomial Pneumonia—Results of a Phase 3, Randomized, Multicenter, Double-Blind, Non-Inferiority Study

Richard G. Wunderink, MD; Richard G. Wunderink, MD; Yuko Matsuhashi, MD; Mari Ariyasu, BPharm; Roger Eichols, MD; Anju Menon, PhD; Tsutae Den Nagata, MD, Shionogi Inc., Florham Park, New Jersey; Shionogi & Co., Ltd. (Employee), Roger Eichols, MD, Shionogi Inc. (Consultant), Anju Menon, PhD, Shionogi Inc. (Employee), Tsutae Den Nagata, MD, Shionogi & Co., Ltd. (Employee).

Session: 83. Late Breaker Oral Abstract Session 1
Thursday, October 3, 2019: 2:15 PM

Background. Cefiderocol (CFDC) is a novel siderophage cephalosporin with activity against a broad range of Gram-negative bacteria. In this study, Day 14 all-cause mortality (ACM) rates were compared between CFDC and meropenem (MEM) in patients with nosocomial Gram-negative pneumonia. The microbiological intent-to-treat population included 156 patients (1 EXE, 1 SoC) were enrolled in the United States. The Day 14 CRR were 70.4% for EXE and 60.0% for SoC groups (p=0.314) overall. In a prespecified analysis of MRSA patients, the CRR with EXE was 74.1% vs. 31.3% with SoC (p = 0.010). Among patients who received study drug, incidence of treatment emergent adverse events (TEAEs) was balanced between groups (24 (88.9%) in EXE and 15 (98.3%) in SoC) as were serious TEAEs (17 (63.0%) in EXE, 12 (75%) in SoC). 1 EXE and 2 SoC US MRSA patients died in hospital. Among US MRSA patients discharged alive from the hospital, the median LOS after study drug was 6 vs. 10 days for EXE and SoC, respectively. Thirty-day AC HRR were 16% vs. 30.8%, for EXE vs. SoC, respectively, and 30-day SA HRR were 8% vs. 15.4%, respectively.

Conclusions. Cefiderocol used in addition to SoC was associated with a reduction in length of hospital stay and 30-day readmission rates for all causes and for S. aureus compared with SoC alone in patients being treated for MRSA bacteremia/endocarditis.

Disclosures. Cara Cassino, MD, ContraFect Corporation (Employee), Hemal Shah, PharmD, Boehringer Ingelheim (Consultant), ContraFect Corp (Consultant), DBV Technologies (Consultant), Mylan specialty (Consultant), NaBrava (Consultant), Joy Lipka-Diamond, MS, ContraFect Corporation (Consultant), Anita F. Das, PhD, Achaogen (Consultant), AntibioiTx (Consultant), Boston Pharmaceuticals (Consultant), Cempra (Consultant), ContraFect Corporation (Consultant), Iterum Therapeutics (Consultant), NaBrava (Consultant), Paratek (Consultant), Tetraphase (Consultant), UTILITY (Consultant), Wockhardt (Consultant).

LB5. A Long-Time Coming: Final 2-year Analysis of Efficacy, Durability, and Microbiome Changes in a Controlled Open-Label Trial of Investigational Microbiota-Based Drug RXB2660 for Recurrent Clostridioides difficile Infections

Robert Orenstein, DO; Sarah Mische, PhD; Sarah Mische, PhD; Ken Blount, PhD; Ken Blount, PhD; Linda Bancke, PharmD; Xin Su, MD, MSE; Dana Walsh, PhD; Adam Harvey, PhD; Carles Gonzalez, MS; Dale N. Gerding, MD; Dale N. Gerding, MD; Mayo Clinic in Arizona, Phoenix, Arizona; Rebiotix Inc., Roseville, Minnesota; Rebiotix Inc., Roseville, Minnesota; BioRankings, LLC, St. Louis, Missouri; Edward Hines Jr. VA Hospital, Hines, Illinois

Session: 83. Late Breaker Oral Abstract Session 1
Thursday, October 3, 2019: 2:25 PM

Background. Recurrent Clostridioides difficile infection (rCdiff) is an urgent public health threat associated with significant mortality and medical cost. Microbiota therapy is gaining acceptance as a strategy to reduce rCDiff recurrence. We present the final 24-month analysis of clinical safety, efficacy, and microbiome restoration from a Phase 2 open-label trial of RXB2660 for prevention of CDI recurrence.

Methods. Participants with multi-recurrent CDI received 2-doses of RXB2660 delivered in enema 7 days apart in this multicenter, open label Phase 2 study. Efficacy was defined as the absence of CDI recurrence through 56 days after the last dose and was compared with 8-week recurrence-free rates for a historical control cohort that received standard-of-care antibiotic therapy. Fisher exact test compared the proportion of treatment participants who were CDI-free by age and sex. Durability was defined as continued absence of CDI episodes beyond 8 weeks. Safety and durability assessments occurred at 3, 6, 12, and 24 months. Participant stool samples were collected prior to and for up to 720 days after treatment, and microbiome changes were assessed by shallow shotgun sequencing.

Results. The efficacy of RXB2660 to prevent rCDI at 8 weeks (78.9%; 112/142) was higher than the CDI-free rate in the historical control group (30.7%, 23/75; P < 0.0001). Age and sex did not impact efficacy. Among participants who achieved treatment success at 8 weeks and were evaluable for long-term durability (n = 95), 8 experienced a new CDI episode by the 24-month follow-up for an overall durability of 91.6%. The safety profile was consistent with previous reports for RXB2660. In total, 503 stool samples from 110 treatment responders were analyzed. Within 7 days of treatment, the relative abundance of Bacteroidia and Clostridia remained shifted.
higher than pre-treatment levels while Gammaproteobacteria and Bacilli declined sharply after treatment, and these changes persisted to at least 24 months.

**Conclusion.** RBX2660, a microbiota-based drug, was safe and efficacious for preventing rCDI with clinical durability to 24 months after treatment, independent of age or sex, and RBX2660 durability associated with durable microbiome shifts from pre-treatment to RSV virus composition.

**Disclosures.** Robert Orenstein, DO, Rebiotix Inc. (Advisor or Review Panel member), Sarah Mische, PhD, Rebiotix Inc. (Employee), Ken Blount, PhD, Rebiotix Inc. (Employee), Lindy Barccke, PharmD, Rebiotix Inc. (Employee), Xin Su, MD, MS, Rebiotix Inc. (Employee), Dana Walsh, PhD, Rebiotix Inc. (Employee), Adam Harvey, PhD, Rebiotix Inc. (Employee), Carlos Gonzalez, MS, Rebiotix Inc. (Consultant), Dale N. Gerding, MD, Rebiotix Inc. (Board Member).

**LB46. EDP-938, a Novel RSV N-Inhibitor, Administered Once or Twice Daily Was Safe and Demonstrated Robust Antiviral and Clinical Efficacy in a Healthy Volunteer Challenge Study**
Eoin Coakley, MD; Alaa Ahmad, PhD; Kaijal Larson, PhD; Ty McClure, PhD; Kai Lin, PhD; Kai Lin, PhD; Kursten Tenhoor, n/a; Kingsley Eze, n/a; Nicolas Noulm, PhD; Veronika Horvathova, MBChB, MSc; Bryan Murray, MBBS; Mark Baillet, PhD; Julie Mori, PhD; Nathalie Adda, MD; Enanta Pharmaceuticals, Boston, Massachusetts; hVIVO Services Ltd., London, UK; S-cubed Biometrics Limited, London, UK.

**Session:** 83. Late Breaker Oral Abstract Session 1
**Thursday, October 3, 2019:** 2:35 PM

**Background.** Respiratory syncytial virus (RSV) represents an important global health challenge with significant morbidity and mortality in infants, elderly, and immunocompromised adults. No effective therapy is currently available. EDP-938 demonstrates potent in vitro activity against RSV Subtypes A and B. We report data from EDP-938-101, a double-blind, placebo-controlled, Phase 2a study that evaluated EDP-938 in adult volunteers inoculated with RSV-A Memphis 37.

**Methods.** Subjects were healthy volunteers, 18–45 years, who were sero-suitable previously if qualitative RT–PCR was RSV+, subjects were randomized to receive 5 days of EDP-938 600 mg once daily (QD arm) or 500 mg loading dose then 300 mg twice daily (BID arm), or placebo twice daily. Assessments included 12 hourly nasal wash monitored for RSV infection by qualitative RSV RT–PCR. On Study Day 5 or (i.e., lower 25th percentile). After RSV inoculation on Study Day 0, subjects had 12 hourly nasal wash for 12 days among RSV-infected subjects, defined as the Intent To Treat-Infected (ITT-I) population. The study was fully powered for both RSV viral load and TSS endpoints.

**Results.** A total of 115 subjects were randomized and inoculated; 86 were included in the ITT-I analysis. The primary and secondary efficacy endpoints were achieved with high statistical significance in QD and BID arms (figure and table). Among EDP-938 recipients all adverse events (AEs) were mild except for a single AE of moderate dyspepsia in the BID arm and events of moderate headache (n = 2) and hypoacusis (n = 1) in the placebo arm. All AEs resolved in follow-up.

**Conclusions.** In the RSV Challenge study, EDP-938 administered once or twice daily achieved primary and key secondary endpoints with robust reductions in RSV viral load (by both qRT–PCR and plaque assays), symptom scores and mucus weights. These data support the further clinical evaluation of EDP-938 in populations at risk of severe RSV disease.

**Disclosures.** Eoin Coakley, MD, Enanta Pharmaceuticals (Employee), Alaa Ahmad, PhD, Enanta Pharmaceuticals (Employee), Kaijal Larson, PhD, Enanta Pharmaceuticals (Employee), Ty McClure, PhD, Enanta Pharmaceuticals (Employee), Kai Lin, PhD, Enanta Pharmaceuticals (Employee), Kursten Tenhoor, n/a, Enanta Pharmaceuticals (Consultant), Kingsley Eze, n/a, hVIVO Services Ltd. (Employee), Nicolas Noulm, PhD, Enanta Pharmaceuticals (Employee), Veronika Horvathova, MBChB, MSc, hVIVO Services Limited (Other Financial or Material Support, Employed by hVIVO during the conduct of the study), Bryan Murray, MBBS, No financial relationships or conflicts of interest, Mark Baillet, PhD, S-CUBED (Employee), Julie Morii, PhD, hVIVO (Employee, Shareholder) Nathalie Adda, MD, Enanta Pharmaceuticals (Employee).

**LB7. A Randomized, Blinded, Placebo- and Vancomycin-Controlled, First-In-Human (FIH) Study of the Safety, Pharmacokinetics (PK), and Fecal Microbiome Effects of ACX-362E, a Novel Anti-Clostridial DNA Polymerase IIIC (polIIIC) Inhibitor**
Kevin W. Garey, MS, PharmD; Kevin W. Garey, MS, PharmD; Martin Kankam, MD, PhD, MPH; Julie Mercier, BS.