weeks. Virologic response, adverse events (AEs), and laboratory abnormalities were evaluated.

Results. Across the two trials, 152 patients without cirrhosis and 16 with compensated cirrhosis received glecaprevir/pibrentasvir for 8 and 12 weeks, respectively. Baseline demographics are shown in Tables 1 and 2. The overall intention-to-treat (ITT) SVR12 rate was 98.2% (165/168), with no virologic failures among non-cirrhotic patients treated for 8 weeks; mITT rate (excluding non-virologic failures) was 99.4% (167/168). Reasons for nonresponse were breakthrough ($n = 1$; patient with incomplete study drug adherence), premature study drug discontinuation ($n = 1$), and missing SVR12 data ($n = 1$). Safety analyses included the additional 18 non-cirrhotic GT1-infected patients treated for 12 weeks (all achieved SVR12). AEs occurring in ≥5% of patients were fatigue, headache, nausea, and nasopharyngitis. Serious AEs and AEs leading to discontinuation were rare; none were related to study drug. Grade 3 or higher laboratory abnormalities were infrequent. All patients maintained HIV-1 suppression (<200 copies/mL) during treatment.

Conclusion. Glecaprevir/pibrentasvir was highly efficacious and well tolerated in patients co-infected with HCV GT1–6/HIV-1 without or with cirrhosis following 8 or 12 weeks of treatment, respectively, and could be the first 8-week pangenotypic treatment option for HCV/HIV-1 co-infected patients without cirrhosis.

Table 1. Baseline Demographics and Disease Characteristics

Characteristic	Without Cirrhosis 8 Weeks N=152	With Cirrhosis 12 Weeks N=16
Male, n (%)	127 (84)	15 (94)
Age, median (range) years	45 (23–74)	50 (35–62)
HCV genotype 1/2/3/4/5/6, n	102/9/22/16/0/3	10/1/4/1/0/0
HCV treatment-experienced, n (%)	31 (20)	2 (13)
HCV RNA, median (range), Log_{10} IU/mL	6.23 (3.98–7.37)	6.05 (4.41–7.03)
CD4+ cell count, median (range), cells/mm^3	595 (154–2103)	545 (222–1806)

Table 2. Baseline Antiretroviral Therapy

Characteristic	Without Cirrhosis 8 Weeks N=152	With Cirrhosis 12 Weeks N=16
Antiretroviral therapy-naïve, n (%)	9 (6)	0
Raltegravir anchor ARV, n (%)	46 (32)[a]	6 (38)
Dolutegravir anchor ARV, n (%)	67 (47)[a]	5 (31)
Rilpivirine anchor ARV, n (%)	30 (21)[a]	5 (31)
ARV = antiretroviral. [a]Denominator excludes patients who are ARV therapy-naïve.		

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1966. Evaluating a Prototype Microbiome Health Index (MHI) as a Measure of Microbiome Restoration Using Data Derived From a Published Study of Fecal Microbiota Transplant (FMT) to Treat Recurrent *Clostridium difficile* Infections (rCDI)

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Session: 227. Clinical Trials
Saturday, October 6, 2018: 12:30 PM

Background. There are efforts to develop FDA-approved microbiota-based drugs to restore the microbiome, notably for recurrent *Clostridium difficile* infections (rCDI). Given the lack of established biomarkers for microbiome restoration, we are evaluating unidimensional Microbiome Health Indices (MHI™). We previously presented a prototype MHI for clinical trials of RBX2660—a standardized microbiota restoration therapy in Phase 3 clinical development. Herein we assessed MHI for a published study of fecal microbiota transplant (FMT) for treating rCDI.

Methods. The prototype MHI is based on the associations of *Bacteroidia* and *Clostridia* with colonization resistance, and *Gammaproteobacteria* and *Bacilli* with dysbiosis, and Receiver Operating Characteristic analysis of pooled RBX2660 trial data indicated that rCDI participants before treatment (baseline) are distinguished from the healthier RBX2660 profile with an odds ratio of 121 (AUC = 0.99, sensitivity = 0.96, specificity = 0.99, cutpoint = 8.2). MHI data for the published FMT cohort were calculated using publicly available data derived from pre- and post-treatment fecal samples (Khanna S, et al. *Microbiome* 2017 **5**:55), and this study included patients with or without a co-diagnosis of inflammatory bowel disease (IBD).

Results. At baseline, 92% of patients in the FMT cohort were below the MHI = 8.2 cutpoint, consistent with a rCDI diagnosis. Among FMT responders 7 days after treatment, 91% of patients had shifted to MHI>8.2, ($P < 0.0001$ compared with baseline). Likewise, a significant shift was observed from baseline to 30 days ($P < 0.0001$), with 83% having MHI > 8.2. There were insufficient patients to support a statistical comparison of IBD vs. no IBD, but MHIs trended lower at all time points among patients with IBD.

Conclusion. MHI parameters derived from RBX2660 trials were predictive of pre- and post-treatment states for a published cohort of FMT-treated rCDI patients, suggesting that this prototype MHI represents a useful dysbiosis measure beyond RBX2660 trials. Lower MHI among patients co-diagnosed with IBD suggests the potential utility of MHI beyond rCDI. Collectively our results continue to support the utility of MHI and its prospective evaluation in ongoing Phase 3 clinical trials.

Disclosures. **K. Blount**, Rebiotix, Inc.: Employee, Salary. **C. Jones**, Rebiotix, Inc.: Employee, Salary. **E. Deych**, Rebiotix, Inc.: Research Contractor, Consulting fee. **B. Shannon**, Rebiotix, Inc.: Research Contractor, Consulting fee.

1967. Study of the Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine (MenACYW-TT) When Co-administered with Other Vaccines in Healthy Adolescents

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Session: 227. Clinical Trials
Saturday, October 6, 2018: 12:30 PM

Background. The MenACYW-TT conjugate vaccine is a quadrivalent meningococcal vaccine candidate intended for global use in all age groups. This pivotal phase II study evaluated the safety and immunogenicity of the vaccine when compared with a licensed quadrivalent conjugated meningococcal vaccine (MCV4-CRM) when co-administered with tetanus, diphtheria, acellular pertussis (Tdap), and human papilloma virus (HPV4) vaccines in meningococcal vaccine naïve adolescents (10–17 years of age).

Methods. A randomized, open-label, multicenter study (NCT02199691) was conducted in 1,715 healthy subjects in the United States, who were randomly assigned to receive MenACYW-TT conjugate vaccine, MCV4-CRM, MenACYW-TT conjugate vaccine (co-administered with Tdap and HPV4), or Tdap and HPV4 vaccines. Serum bactericidal assay with human (hSBA) and baby rabbit (rSBA) complement was used to measure antibodies against serogroups A, C, W, and Y test strains at baseline and 30 days after vaccination. Safety data were collected up to 6 months post-vaccination.

Results. Noninferiority of immune response was demonstrated between MenACYW-TT conjugate vaccine and MCV4-CRM, and MenACYW-TT conjugate vaccine when co-administered with Tdap and HPV4 vaccines vs. when administered alone, based on percentages of study participants achieving hSBA vaccine seroresponse at Day 30 fromD0 baseline. The proportions of individuals with hSBA ≥ 1:8 after MenACYW-TT conjugate vaccine administration were higher than those after MCV4-CRM administration for all four serogroups (A: 93.5% vs. 82.8%; C: 98.5% vs. 76.0%; W: 99.1% vs. 90.7%; Y: 97.2% vs. 83.2%). Co-administration of MenACYW conjugate, Tdap and HPV4 vaccines did not generate any results suggestive of immune interference. Reactogenicity profiles were comparable across study groups. Most unsolicited adverse events were of Grade 1 or Grade 2 intensity. No vaccine related serious adverse events were reported.

Conclusion. MenACYW-TT conjugate vaccine was immunogenic and well tolerated when administered as a single dose to meningococcal vaccine naïve adolescents along with Tdap and HPV4 vaccines. Such a vaccine will offer an alternative for the prevention of invasive meningococcal disease in susceptible populations across the world.

Disclosures. **All authors:** No reported disclosures.

1968. Procalcitonin-Guided Antibiotic Therapy for Lower Respiratory Tract Infections in a US Academic Medical Center

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Session: 227. Clinical Trials
Saturday, October 6, 2018: 12:30 PM

Background. European trials using procalcitonin (PCT)-guided antibiotic therapy for patients with lower respiratory tract infections (LRTI) have resulted in significant reductions in antibiotic use without increasing adverse outcomes. Few prospective studies have examined PCT-guided antibiotic therapy for LRTI in the United States.

Our objective was to examine whether an PCT algorithm compared with standard practice would reduce antibiotic exposure in patients with LRTI [pneumonia and acute exacerbations of chronic obstructive pulmonary disease (AECOPD)] in an American urban academic hospital.

Methods. From April 17, 2017 until November 1, 2017, consecutive patients admitted to a medicine service were enrolled in the PCT intervention if they were receiving antibiotics for LRTI and gave consent. Providers were encouraged to discontinue antibiotics using a PCT algorithm with predefined cutoffs. Serum PCT was measured in the hospital laboratory once daily. Results and recommendations were communicated to providers by study team and in the medical record. Control patients were selected by reviewing charts for patients admitted to a medicine service for LRTI from December 1, 2016 to April 16, 2017. The primary endpoint was median antibiotic duration. Overall adverse outcomes at 30 days comprised death, transfer to an intensive care unit, antibiotic side effects, *Clostridium difficile* infection, disease- specific complications, and new antibiotic prescription for LRTI after discharge.

Results. 174 patients were enrolled in the intervention group and 200 patients in the control group. Intervention group providers complied with the PCT algorithm in 75% of encounters. The rate of overall adverse outcomes was similar in PCT and control groups (21.8% vs. 23.5%; difference, –0.02; 95% CI, –0.10 to 0.07). PCT-guided therapy reduced the median antibiotic duration for pneumonia from 7 days to 6 (P = 0.05), and AECOPD from 4 days to 3 (P = 0.01). Noncompliance with the PCT algorithm resulted in 260 excess antibiotic days in 44 patients.

Conclusion. In our center, 75% adherence to a PCT-guided algorithm safely reduced the duration of antibiotics for treating LRTI. Incentivizing providers to comply with PCT-guided algorithms could lead to further reductions in antibiotic use.

Disclosures. **J. Townsend**, BRAHMS: Grant Investigator, Research grant.

1969. Comparison of Adverse Event Rates Between Patients Treated With Ceftaroline or Ceftriaxone

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Session: 227. Clinical Trials
Saturday, October 6, 2018: 12:30 PM

Background. At the VA St. Louis Health Care System 17.3% of patients treated with ceftaroline developed an adverse drug reaction (ADR). This evaluation compares ADR rates between patients treated with ceftaroline and those treated with ceftriaxone.

Methods. This was a retrospective, single-center cohort study of patients treated with ceftaroline or ceftriaxone at the VA St. Louis Health Care System between October 29, 2010 and March 28, 2017. Patients included received at least two doses of either medication and were treated for osteomyelitis, acute bacterial skin and skin structure infections, blood stream infections, pneumonia, infective endocarditis, septic arthritis, prosthetic joint infections, or an empyema. Once identified, patients were matched 1:1 utilizing the nearest neighbor method accounting for age, indication, and duration of therapy. The primary and secondary outcomes were the composite of any ADR while on therapy and any ADR leading to therapy discontinuation, respectively. Adverse reactions evaluated were rash, neutropenia, acute kidney injury, eosinophilia, thrombocytopenia, transaminitis, and hyperbilirubinemia.

Results. There were 75 unique ceftaroline-treated and 312 ceftriaxone-treated patients identified. After propensity score matching, 50 patients per group were included and analyzed. The mean age of patients was 65.4 and 63.4 years (P = 0.47), and the mean duration of therapy was 14.5 and 17 days (P = 0.90), ceftriaxone compared with ceftaroline respectively. Any ADR occurred in 20% (10/50) of patients treated with ceftriaxone and 16% (8/50) of patients treated with ceftaroline (P = 0.60). One patient (2%) treated with ceftriaxone and 16% (8/50) treated with ceftaroline had therapy discontinued for an ADR (P = 0.03). The most common ADR was eosinophilia (3/50) in the ceftriaxone group and rash (5/50) in the ceftaroline group. In multivariate regression, ceftaroline therapy was identified as an independent risk factor for development of an ADR requiring discontinuation (OR 10.2; 95% CI 1.19–87.8), P = 0.03).

Conclusion. There was no difference in the development of any ADR between patients treated with ceftriaxone or ceftaroline, but patients treated with ceftaroline had more ADRs leading to therapy discontinuation.

Disclosures. **All authors:** No reported disclosures.

1970. Phase 1 Clinical Trial of Intranasal Immunization with M2-Deficient, Single Replication, Live Influenza Vaccine (M2SR): Safety and Immune Response in Adults

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Session: 227. Clinical Trials
Saturday, October 6, 2018: 12:30 PM

Background. Influenza vaccines are needed with greater effectiveness and breadth of coverage. FluGen is developing M2SR (*M2* deficient Single *R*eplication), an investigational, live virus vaccine. M2SR contains the internal proteins of donor A/Puerto Rico/8/34 and hemagglutinin (HA) and neuraminidase (NA) selected from targeted Type A influenza strains. M2SR undergoes only a single round of infection in the respiratory epithelium but evokes an immune response profile similar to wild-type influenza viruses. In influenza naïve and pre-immune ferrets, M2SR protects against multiple influenza A subtypes.

Methods. A Phase 1, first-in-human, randomized, placebo-control study (FluGen-H3N2-V001; ClinicalTrials.gov identifier NCT02822105) was conducted at a single USA site, with 96 adults, ages 18–49 years. Study vaccine contained HA and NA from A/Brisbane/10/2007 (H3N2). Study volunteers received a single intranasal (IN) inoculation with either M2SR at dose levels of 10^6, 10^7 or 10^8 $TCID_{50}$ or saline placebo (N = 24/cohort). Study subjects were evaluated for virus replication and solicited local and systemic reactions for 7 days, all adverse events (AE) for 28 days and serious AE (SAE) for 180 days.

Results. No infectious virus was detected in nasal swabs from any vaccinated subject. The most commonly reported AE was mild nasal rhinorrhea/congestion during the first 7 days after vaccination (Figure 1). No subject had fever or a severe reaction to the vaccine. No SAEs were reported. At least one AE was reported among 29%, 58%, and 83% of M2SR subjects administered 10^6, 10^7, or 10^8 $TCID_{50}$, respectively, and 46% among placebo subjects. There were no notable imbalances among study groups for other events. T- and B-cell responses, including influenza-specific serum and mucosal antibody responses were detected at a significantly higher frequency among vaccine than placebo subjects (Figure 2).

Conclusion. M2SR vaccine was safe and well tolerated at all dose levels, generated a dose-response effect for humoral (HA antibody) and mucosal antibodies against both homologous and heterologous influenza variants, and elicited robust T-cell responses. No infectious virus was detected in nasal swabs from any vaccinated subject.

Figure 1. Common adverse events first 7 days post-vaccination

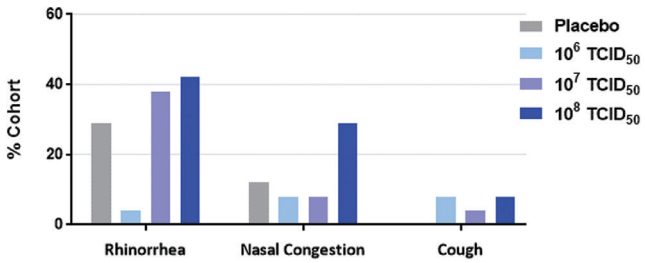

Figure 2. Influenza-specific immune responses

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