Conclusion. CAZ-AVI is a potential therapeutic option for treating respiratory infections in the Asia/Pacific region caused by Ebs and Fae isolates resistant to commonly used and last-in-line agents.

Disclosures. G. G. Stone, Pfizer: Employee, Salary AstraZeneca: Shareholder, Capital Gains

1244. Activity of Ceftolozane-Tazobactam Against Global Pseudomonas Aeruginosa and Non-Susceptible Phenotypes: SMART 2016

Sybille Lob, MD, MPhil, Robert Badal, BS1;
Katherine Young, MS2; Mary Motyl, PhD3 and Dan Sahm, PhD1; International Health Management Associates, Inc., Schaumburg, Illinois, ‘Merck & Co., Inc.; Kenilworth, New Jersey

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing Friday, October 6, 2017: 12:30 PM

Background. Pseudomonas aeruginosa (PA), one of the species of the ESXPAE pathogens that are known to “escape” the effects of many antimicrobials, is often difficult to treat. Cefotolozane-tazobactam (C/T) is an anti-pseudomonal cephalosporin/b-lactamase inhibitor recently approved by FDA and EMEA. We examined its activity against global clinical isolates of PA, including isolates non-susceptible (NS, intermediate or resistant) to other agents.

Methods. In 2016, 158 hospitals in 51 countries collected 5533 PA from intra-abdominal (IAI), urinary (UTI), and respiratory tract infections (RTI). MICs were determined using CLSI broth microdilution and interpreted with both CLSI and EUCAST breakpoints, as the susceptible breakpoints for C/T, cefepime (FEP), meropenem (MEM), and piperacillin-tazobactam (P/T) are the same using both criteria.

Results. Overall susceptibility of PA to C/T, prevalence of FEP-NS, MEM-NS, and P/T-NS phenotypes, and susceptibility of these phenotypes to C/T are shown below:

| Region       | Total | C/T susceptibility (%) | PA, FEP-NS | PA, MEM-NS | PA, P/T-NS |
|--------------|-------|------------------------|------------|------------|------------|
| All PA (n)   | 405   | 87.9                   | 111 (27.4) | 138 (34.1) | 124 (30.6) |
| [n(% of total)] |       | [n(% of total)] | [n(% of total)] | [n(% of total)] |
| Africa       | 66.1  | 69.1                   | 73.3       | 57.9       | 62.1       |
| Asia*        | 66.6  | 69.1                   | 73.3       | 57.9       | 62.1       |
| Europe       | 72.2  | 68.8                   | 72.2       | 58.1       | 72.6       |
| Latin America| 85.5  | 85.5                   | 85.5       | 85.5       | 85.5       |
| Middle East  | 85.5  | 85.5                   | 85.5       | 85.5       | 85.5       |
| North America| 86.6  | 86.6                   | 86.6       | 86.6       | 86.6       |
| South Pacific| 88.6  | 88.6                   | 88.6       | 88.6       | 88.6       |

* Does not include China or India

Differences in C/T susceptibility across isolates from IAI (91.4%), RTI (90.5%), and UTI (89.3%) were small.

Conclusion. Overall susceptibility to C/T ranged from 85% in Latin America to 98% in South Pacific. FEP-NS, MEM-NS, and P/T-NS isolates were least prevalent in South Pacific. C/T was active against these phenotypes in >80% of isolates in North America and South Pacific and against 62–73% of MEM-NS and P/T-NS isolates in all other regions except Latin America. Monitoring of C/T susceptibility to PA was warranted in light of increasing resistance to first-line agents.

Disclosures. M. Hackel, HIMHA: Employee, Salary; R. Badal, HIMHA, Inc; Employee, Salary; K. Young, Merck: Employee and Shareholder, Dividends and Salary M. Motyl, Merck & Co., Inc.; Employee, Salary

1245. Genome Wide Analysis Reveals Host Genetic Variants that Associate with Reduction in Clostridium difficile Infection Recurrence (rCDI) in Patients Treated with Bezlotoxumab

Peter Shank, PhD1; Judong Shen, PhD2; Mary Beth Dorr, PhD3; Mark Wilcox, MD4; Junhua Li, PhD5; Robin Mogg, PhD6; Devan V. Mehrora, PhD1 and Rebecca L Blanchard, PhD1; ‘Merck & Co., Inc., Kenilworth, New Jersey, 2Leeds Institute of Biomedical and Clinical Sciences, University of Leeds, Leeds, United Kingdom, 3BGI-Shenzhen, Shenzhen, China

Session: 148. C difficile: From the Bench to Bedside Friday, October 6, 2017: 12:30 PM

Background. Bezlotoxumab (BEZ) and actoxumab (ACT) are monoclonal antibodies against C. difficile toxins B and A, respectively. Patients receiving a single infusion of BEZ alone or with ACT in the MODIFY I/II trials showed a consistent reduction in the rate of rCDI over a 12-week period compared with a placebo (PBO) infusion. Exploratory genome wide analyses were conducted to determine whether genetic variants across the genome were associated with treatment response (rCDI).

Methods. DNA was extracted from blood obtained from patients who consented to genetic analysis (PGx population). Genetic data were generated on a commercial Axiom array platform (Affymetrix). Genotype imputation was performed using the 1000 Genomes Phase 3 reference data and imputed software after genetic quality control. Data from BEZ and ACT+BEZ arms were combined to provide increased power. The logistic regression with likelihood ratio test was used to search for single nucleotide polymorphisms (SNPs) that were strongly associated with a treatment effect on rCDI.

Results. An SNP rs2516513 located in the extended major histocompatibility complex (xMHC), region with a minor allele frequency of 25% in the general population, was associated with rCDI (P = 3.04E-08) (Figure 1). rCDI rates for the PGx population and in subgroups at high/low risk for rCDI stratified by SNP rs2516513 are shown in Table 1. Carriers of the T allele of SNP rs2516513 were associated with a statistically significant reduction in rCDI in BEZ-treated patients but not in PBO-treated patients (DrCDI = -21.5%). The magnitude of the effect of the T allele on rCDI is most prominent in patients who have ≤1 risk factor for rCDI (DrCDI = -24.6%), but is also present in patients without risk factors (DrCDI = -10.6%). In CC homozygous patients, rCDI rates are similar in both treatment groups and in patients at high and low risk of rCDI.

Conclusion. An SNP variant rs2516513 is associated with a lower rate of rCDI recurrence in patients treated with BEZ. The location of the associated genetic variant on chromosome 6 within xMHC, suggests that a host driven, immunological mechanism may play a role in rCDI and may predict patients most likely to respond to BEZ. As this is an exploratory finding, the results should be replicated in an independent validation study.

Figure 1. Manhattan plot of the p-values of the genome wide associations SNPs and treatment effect on rCDI

Table 1. Proportion of Patients with rCDI stratified by SNP rs2516513 genotype and by risk category

| Genotype | BEZ and ACT+BEZ | PBO | Difference (%) |
|----------|----------------|-----|---------------|
| CC       | 36 (78.4%)     | 38 (79.6%) | -3.2 |
| CT or TT | 32 (67.3%)     | 35 (72.3%) | -5.0 |

| High Risk* | 31.5 [69 (21/193)] | 38.8 [78 (39/199)] | -4.3 |
| Low Risk   | 32.7 [65 (25/27)]  | 33.3 [75 (25/27)]  | 0.6 |

Disclosures. P. Shank, Merck & Co., Inc.: Employee, May own stock/hold stock options in Company; J. Shen, Merck & Co., Inc.: Employee, May hold stock/hold stock options in the Company; M. B. Dorr, Merck & Co., Inc.: Employee and Shareholder, may own stock/hold stock options in the Company; J. L. Blachard, Merck & Co., Inc.: Employee, May own stock/hold stock options in the Company; D. V. Mehrora, Merck & Co., Inc.: Employee, May own stock/hold stock options in the Company; R. L. Blachard, Merck & Co., Inc.: Employee, May own stock/hold stock options in the Company

1246. Engraftment and Augmentation of Microbiome Following Fecal Microbiota Transplantation for Recurrent Clostridium difficile Infection

Christine Lee, MD, FRCP(C); Stephen Rush, PhD1; J. Scott Weese, DVM1; Peyman Goldshtein, B.Eng2 and Peter Kim, PhD3; 1Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada, 2University of Guelph, Guelph, ON, Canada, 3Microbiology, University of Guelph, Ontario Veterinary College, Guelph, ON, Canada, 4Vancouver Island Health Authority, Victoria, BC, Canada, 5Mathematics and Statistics, University of Guelph, Guelph, ON, Canada

Session: 148. C difficile: From the Bench to Bedside Friday, October 6, 2017: 12:30 PM

Background. Bezlotoxumab (BEZ) and actoxumab (ACT) are monoclonal antibodies against C. difficile toxins B and A, respectively. Patients receiving a single infusion of BEZ alone or with ACT in the MODIFY I/II trials showed a consistent reduction in the rate of rCDI over a 12-week period compared with a placebo (PBO) infusion. Exploratory genome wide analyses were conducted to determine whether genetic variants across the genome were associated with treatment response (rCDI).

Methods. DNA was extracted from blood obtained from patients who consented to genetic analysis (PGx population). Genetic data were generated on a commercial
Background. Recurrent Clostridium difficile infection (rCDI) poses major challenges to healthcare providers and patients. Fecal Microbiota Transplantation (FMT) is an effective therapy for rCDI, but the exact mechanism of its efficacy is unknown. Current metagenomics literature indicates that abundance of Bacteroides and Firmicutes may protect against CD proliferation and recurrence. However, this is too broad to be useful for developing refined and targeted microbial-specific therapy for rCDI, because the long-term safety of FMT remains unknown. We examined the phylogeny of bacteria pre- and post-FMT to determine the key organisms associated with successful FMT to the genera level.

Methods. A subset of patient stool samples (n = 35) from a phase 2 study comparing fresh vs. frozen FMT was sequenced at four time points: pre-FMT; at day 10; at week 5; and at week 13, following the last FMT. The matching donor stool was sequenced simultaneously with the corresponding patients’ pre- and post-FMT samples.

Using the binary outcome to a single FMT assignment as the response, we developed an in-house machine learning algorithm, FLASSO, to isolate key genera using the bacterial phylogenetic structure.

Engraftment was defined as: newly detected operational taxonomic unit (OTU) appearance in the patient post-FMT, which were present in the donor but undetected in the patient pre-FMT. Augmentation was defined as: non-donor OTUs whose levels substantially increased post-FMT. Figure 1 (below) displays the distribution of engrafted and augmented OTUs at varying thresholds. We observed increases over time points within each threshold level.

Results. Akkermansia, Blautia and Roseburia appear to be key genera for successful FMT. The FLASSO fits with consistently positive coefficients, see Figure 2.

Conclusion. In this preliminary study, using FLASSO, we have shown that specific microbes to the genera level are uniformly present in successful FMT. This information may lead to developing refined and targeted microbial therapy for future patients.

1247. Lyophilized Fecal Microbiota Transplantation Capsules for Recurrent Clostridium difficile Infection

Herve Dupont, MD1; Zi-Dong Jiang, MD, DrPH2; Ashley Alexander, MHS3; Nadim Ajami, PhD4; Joseph F. Petrosino, PhD5; Andrew W. DuPont, MD, MS6; Shi Ke, MD7; Goo Jun, PhD8 and Craig Harms, PhD9; UT School of Public Health, Houston, Texas; The University of Texas Houston School of Public Health, Houston, Texas; 3Baylor College of Medicine, Houston, Texas; 4Department of Molecular Virology and Immunology, Baylor College of Medicine, Houston, Texas; 5Internal Medicine, University of Texas Medical School, Houston, Texas; 6Georgia Public Health, Atlanta, Georgia; 7University of Texas School of Public Health, Houston, Texas; 8University of Texas School of Public Health, Houston, Texas; 9University of Texas School of Public Health, Houston, Texas

Session: 148. C. difficile: From the Bench to Bedside

Friday, October 6, 2017: 12:30 PM

Background. Fecal microbiota (FM) transplantation (FMT) is a highly effective treatment of recurrent C. difficile infection (rCDI). We have published data showing efficaciousness of fresh, lyophilized and encapsulated lyophilized donor microbiota administered by colonoscopy. Most groups are moving toward use of frozen product given by enema and in evaluating encapsulated product for oral delivery.

Methods. This was a prospective, randomized study of subjects with rCDI (≥ 3 episodes) treated with encapsulated lyophilized FM 100 g given once or 100 g given on two successive days (total 200 g) vs. frozen FM product 100 g given by single retention enema, between March 2015 and February 2017. The clinical outcome was absence of CDI during the 60 days after FMT. The subjects were followed for 6 months for safety. In a subset recipients, microbiome composition by 16S rRNA gene profiling were analyzed on stools obtained pre- and day 2, 7, 14, 30, 60 and 90 days after FMT.

Results. A total of 54 subjects were enrolled (37/54; 69% female) with a median age of 71 years (range: 20–97). In the first 14 subjects treated, cure rates for oral capsules 100 g FM was 5/8 (63%) vs. 6/6 (100%) for those receiving 100 g freezing FM by enema (P = 0.239). In the second phase of the study cure rate for oral capsules 200 g FM was 17/18 (91%) vs. 20/21 (94%) for the subjects treated by enema by 100 g of frozen product (P = 0.782). No side effects were felt to be related to the procedure or the FMT products were recorded during 6 months follow-up. Two subjects died having follow-up between 3 and 6 months after study due to underlying medical conditions felt to be unrelated to FMT. Microbiota analysis were performed on 40 subjects of which 19/40 (48%) had received capsules. Figure showed that restoration of the intestinal microbiome diversity and Taxa began apparent 2 days after FMT in both groups and resembled the donor product by 2 weeks with stabilization of the microbiota diversity and Taxa persisting for the 90 days of observation.

Conclusion. Administration of encapsulated, lyophilized FM resulted in durable restoration of intestinal microbiome diversity comparable to results seen with frozen product given by enema.

1248. Socioeconomic Status Factors Associated with Increased Incidence of Community-Associated Clostridium difficile Infection

Kimberly Skzobareck, MD1; Yi Mu, PhD2; Lisa G. Winston, MD3; Geoff Broussaud, MPH4; Carol Lyons, MS5; MPH5; Monica Farley, MD, FIDSA6;becca Permutler, MPF7; Stacy Holzbaumer, DVM, MPH, DACVP8; Erin C. Phypaps, DVM, MPH9; Chinowa Dumnyati, MSF10; Zintars G. Beldavs, MSF11; Marion Kaiser, MBBS12, MPH13, FE14; and Alice Guh, MD, MPH15; Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; 3Medicine, University of California, San Francisco and Zuckerberg San Francisco General Hospital and Trauma Center, San Francisco, California; 4Colorado Department of Public Health and Environment, Denver, Colorado; 5Yale School of Public Health, Connecticut Emerging Infections Program, New Haven, Connecticut; 6Department of Medicine, Emory University School of Medicine and Atlanta VA Medical Center, Atlanta, Georgia; 7Maryland Department of Health and Mental Hygiene, Baltimore, MD; 8Minnesota Department of Health, St. Paul, Minnesota; 9University of New Mexico, New Mexico Emerging Infections Program, Albuquerque, New Mexico; 10New York Emerging Infections Program at the University of Rochester Medical Center, Rochester, New York; 11Oregon Health Authority, Portland, Oregon; 12Tennessee Department of Health, Nashville, Tennessee

Session: 148. C. difficile: From the Bench to Bedside

Friday, October 6, 2017: 12:30 PM

Background. Traditionally a hospital-acquired pathogen, Clostridium difficile is increasingly recognized as an important cause of diarrhea in community settings. Health disparities in C. difficile infection (CDI) have been reported, but little is known about the social determinants of health that influence community-associated (CA) CDI incidence. We sought to identify socioeconomic status (SES) factors associated with increased CA-CDI incidence.

Methods. Population-based CDI surveillance is conducted in 35 U.S. counties through the Centers for Disease Control and Prevention’s Emerging Infections Program. A CA-CDI case is defined as a positive C. difficile stool specimen collected as an outpatient or within three days of hospitalization in a person aged ≥1 year who did not have a positive test in the prior 8 weeks or an overnight stay in a healthcare facility in the prior 12 weeks. ArcGIS software was used to geocode 2014–2015 CA-CDI case addresses to a 2010 census tract (CT). Incidence rate was calculated using 2010 Census population denominators. CT-level SES factors were obtained from the 2011–2015 American Community Survey 5-year estimates and divided into deciles. To account for CT-level clustering effects, separate generalized linear mixed models with negative binomial distribution were used to evaluate the association between each SES factor and CA-CDI incidence, adjusted by age, sex and race.

Results. Of 9686 CA-CDI cases, 9417 (97%) had addresses geocoded to a CT; of these, 62% were female, 82% were white, and 35% were aged ≥65 years. Annual CA-CDI incidence was 42.9 per 100,000 persons. After adjusting for age, sex and race, CT-level SES factors significantly associated with increased CA-CDI incidence included living under the poverty level (rate ratio [RR] 1.12; 95% confidence interval [CI] 1.09–1.15), crowding in homes (RR 1.11; 95% CI 1.01–1.21), low education (RR 1.11; 95% CI 1.07–1.15), low income (RR 1.15; 95% CI 1.12–1.17), having public health insurance (RR 1.21; 95% CI 1.18–1.24), receiving public assistance income (RR 1.69; 95% CI 1.55–1.84), and unemployment (RR 1.14; 95% CI 1.07–1.22).

Conclusion. Areas with lower SES have modestly increased CA-CDI incidence. Understanding the mechanisms by which SES factors impact CA-CDI incidence could help guide prevention efforts in these higher-risk areas.

Disclosures. All authors: No reported disclosures.

1249. Prevalence of Clostridium difficile and Multidrug Resistant Gram-negative Rods in the Soil from Southeastern Wisconsin

Angela Loo, NA1; Cathy Tran, NA1; Annette Jenson, BMSTT/ASC/SM5, CKC; Jennifer Califumin, BS4; Curtis Donkey, MD5 and L. Silva Monoz-Price, MD, PhD3; Divine Savior Holy Angels High School, Milwaukee, Wisconsin; 2Research Service, Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio; 3Research Service, Cleveland VA Medical Center, Cleveland, Ohio; 4L. Stokes Cleveland VA Medical Center, Cleveland, Ohio; 5Medical, Medical College of Wisconsin, Milwaukee, Wisconsin

Session: 148. C. difficile: From the Bench to Bedside

Friday, October 6, 2017: 12:30 PM

Background. Traditionally a hospital-acquired pathogen, C. difficile might be more common in rural areas. Thus, farms—specifically livestock...