Methods. IDXV were produced by co-transfection of transfer, packaging, and envelope plasmids in 293T cells and purification on sucrose gradients. IDXV were normalized using a colorimetric reverse transcriptase assay. Plasmid expressing mAb VN04-2 was provided by B. Hanson. mAb in the supernatant of transfected cells were detected by western blot and quantified by the Easy-Titer Human IgG Assay Kit. For in vivo studies, groups of 6–8 weeks old mice were received IDXV either by intranasal (in) or intramuscular (im) route. mAb production was detected by western blot and ELISA. Mice were challenged using the recombinant IAV VNHSV1-PR8/CDC RG derived from IAV A/Vietnam/1203/2004.

Results. We engineered IDXV producing the humanized mAb VN04-2 (IDXV-VN4-2), which is broadly neutralizing against H5 IAV. We found that after transduction of 293T cell with different dosages IDXV-VN4-2, the production of mAb was time and dose dependent. mAb were also functional, and bind specifically H5 HA but not other IAV proteins. We also measured VN04-2 production in the serum of mice, 3, 6, 9, 14, 21 and 30 days after in or im administration of IDXV-VN4-2. We found that levels of mAb were sustained. In separate experiments 5/5 mice receiving IDXV-VN4-2 by the in route and 2/5 mice receiving it by the im route were protected from lethal IAV challenge.

Conclusion. Our data suggest that IDXV may represent an attractive candidate for vector-mediated immunization against infectious disease.

Disclosures. All authors: No reported disclosures.

1660. Antiviral Activity of Peptide Nucleic Acid against Human Parechovirus Type 3
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Background. Human parechovirus (HPeV) type 3 (HPEV3) is an emerging pathogen, and spread between households and, especially, other HCPs among neonatal intensive care unit (NICU). However, specific treatment for HPEV3 infection is currently unavailable. The application of anti-sense technology, such as peptide nucleic acids (PNAs), to viral infection has opened the door to PNA expression in an in vitro model.

Methods. We designed four PNAs that target domains I, J (base and head of the 5' untranslated region of HPEV3. The IRES region is needed for the cap-independent translation. The PNAs were conjugated to cell-penetrating peptide (RXR)XB (R = L-arginine, X = 6-aminohexanoic acid, B = β-alanine), LLC-MK2 cells were treated with 0.1–10µM of each PNA or water/control growing medium for 4h. The cells were then infected with HPEV3 at the multiplicity of infection (MOI) of 10 for 1h. The infected cells were incubated for 7 days at 37°C in 5% CO2. Extracellular levels of HPEV3 RNA were measured by real-time PCR on days 0 and 7.

Results. Without any treatment, an extracellular level of HPEV3 RNA increased to 8.2 × 10^6 copies/µL on day 7. When the cells were treated with 10µM of PNA targeting the domain I of IRES, an extracellular level of HPEV3 RNA was suppressed to 4.7 × 10^6 copies/µL (−99%) on day 7. Using the same PNA with lower concentration, 1 µM and 0.1 µM of the PNA suppressed 24% and 0% of extracellular levels of HPEV3 RNA, respectively, which demonstrated the effect is dose-dependent. In contrast, 10µM of PNAs targeting domain J (base), J (head), and K suppressed 94%, 92%, and 32% extracellular levels of HPEV3 RNA respectively, compared with control.

Conclusion. The PNA (RXR)XB targeting the domain I of IRES suppressed extracellular levels of HPEV3 RNA in an in vitro model in a dose-dependent manner. Thus, PNA treatment may be a therapeutic candidate for HPEV3-infected patients. This novel therapy could target other HPeV genotypes given that the target sequence used in this study is identical to those of other clinically significant HPeVs.

Disclosures. All authors: No reported disclosures.

1661. Preventing Respiratory Viruses in the Neonatal ICU
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Background. Infants in the neonatal ICU can acquire respiratory viruses from ill healthcare personnel (HCP), visitors, or other infants. We describe the epidemiology of respiratory viruses and infection prevention and control interventions aimed to reduce acquisition and transmission of respiratory viruses in our NICU.

Methods. From May 2011 to December 2016, we tracked respiratory viruses detected by a multiplex reverse-transcriptase (RT)-PCR assay (FilmArray, Biofire, Inc.) in our 58-bed level IV NICU (~1,000 annual admissions). Testing was ordered for clinicians treating for symptomatic infants. Infants with positive RT-PCR tests generally remained on contact/ droplet precautions throughout their NICU stay. IPCP were contacted as sick and report to Workforce Health and Safety if they became ill at work. Ill visitors were not permitted in the NICU, as enforced by written educational materials and signage, but formal screening was not performed. Starting in January 2015, asymptomatic infants exposed to RT-PCR-positive index cases were screened by RT-PCR, put on contact/ droplet precautions for the incubation period (IP) of the index case’s virus, and screened again at IP end. Starting in December 2015, infants more than 4 weeks old were screened. We assessed nosocomial respiratory illness events (2 infants), clusters (3 infants), and outbreaks (>3 infants); all were defined as detecting geographically related cases within the relevant IP. We determined screened infants who had positive RT-PCR tests.

Results. During the 5-month observation period, 79 infants had 83 viruses detected (~18% of admissions). Rhinovirus/enterovirus (RV/EV) were most common (n = 59) and caused 1 outbreak of 7 infants, 4 clusters, and 5 dyad transmissions. Adenovirus caused 1 outbreak of 5 infants. Two dyad transmissions occurred for parainfluenza. Apoactic cases of RSV (n = 5), coronavirus (n = 2), and influenza (n = 2) occurred. Three household contacts were identified for 10 infants. No HCPs were identified with respiratory illnesses. Since January 2015, 8 screened infants had positive RT-PCR tests. Since December 2015, only 1 transmission dyad (RV/EV) occurred.

Conclusion. Preliminary data suggest that our interventions have reduced the burden of respiratory viruses in the NICU.

Disclosures. All authors: No reported disclosures.

1662. Use of Oral Ribavirin for the Treatment of RSV Infections in Hematopoietic Cell Transplant (HCT) Recipients
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Background. The benefit of aerosolized ribavirin (AR) in reducing the risk of progression of RSV infections and RSV-associated mortality in HCT recipients has been recognized, yet there is paucity of data assessing the use of oral ribavirin (OR) in this patient population. We evaluated outcomes associated with the use of OR compared with AR in HCT recipients.

Methods. Retrospective review of all HCT recipients with RSV infection treated with OR or AR during three RSV seasons (September 2014 – February 2017). An established immunodeficiency Scoring Index (ISI) was applied to identify patients at high risk for progression and death based on host risk factors. Mortality, progression to lower respiratory infection (LRI), and need for ICU admission was compared among recipients of AR and OR.

Results. A total of 107 patients were treated with OR (n = 42, 39%) or AR (n = 65, 61%). Recipients of AR and OR were equally likely to be high-risk by ISI scoring (11% vs. 10%, P = 1.00). Fifty-three patients (50%) presented with upper respiratory infection (URI) of whom 13 (25%) progressed to LRI. There was no difference in the rate of progression to URI and LRI between patients who received OR vs. AR (8% vs. 18%, P = 0.53). No difference was found in 30-day mortality rates based on treatment strategy (8% for AR vs. 5% OR, P = 0.70). Interestingly, 90-day mortality was found to be significantly lower among patients who received OR vs. AR (20% vs. 5%, P = 0.04). No difference in rate in rates of ICU admission and requirement for mechanical ventilation was found between the two groups. For the 99 inpatients at time of diagnosis, median (interquartile range) length of stay was 7 (5–19) days, and was similar for patients on either treatment modality. Eight patients were treated for RSV on an outpatient basis and all received OR.

Conclusion. HCT patients with RSV had similar outcomes when treated with AR vs OR, AR or OR may be a safe and effective alternative for AR for prevention and treatment of RSV in HCT patients with significantly reduced cost.

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1829. Pharmacokinetis (PK) of Evaraclyine in Subjects with Renal or Hepatic Impairment Compared with Healthy Subjects
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Session: 231. Clinical Study with New Antibiotics and Antifungals
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Background. Evaraclyine (ERV) is a fluorocycline being developed for the treat- ment of serious infections, including those caused by multidrug-resistant pathogens. The PK of ERV in subjects with end stage renal disease (ESRD) or hepatic impairment (HI) were investigated.
Methods. Two multi-center studies were completed; one in subjects with ESRD and one in subjects with mild, moderate or severe HI based upon Child-Pugh scoring. Each included a cohort of healthy subjects (HS) matched by gender, age and BMI. A single IV dose of 1.5 mg/kg ERV was administered. PK parameters were calculated using standard non-compartmental methods and within study comparisons of PK for the ESRD and HI subjects were made with HS.

Results. The following comparative AUC₀₋₄₄ and C₀₋₄₄ values for ERV were observed:

| Subjects Status (n) | ESRD (6) vs. HS (6) | Mild (4) vs. HS (5) | Severe (6) vs. HS (6) | C₀₋₄₄ (ng/mL) | Ratio of AUC₀₋₄₄ (%) | Mean 90% CI for ratio (%) | Intra-subject CV (%) |
|---------------------|---------------------|--------------------|---------------------|----------------|---------------------|-------------------------|---------------------|
| ESRD (6) vs. HS (6) | 96  (82, 112)       | 52  (49, 55)       | 54  (45, 63)       | 15            | 109                | 109                     | 30                  |
| Mild (4) vs. HS (5) | 123               | 90                | 125               | 32            | 138                | 138                     | 32                  |
| Severe (6) vs. HS (6) | 210               | 100               | 125               | 30            | 114                | 114                     | 30                  |

Conclusion. Following a single IV dose of ERV, the systemic exposures in subjects with ESRD and mild or moderate hepatic impairment were similar to those observed in HS. The 2-fold increase in AUC₀₋₄₄ observed in subjects with severe HI did not result in increased adverse events. Therefore, no dose adjustment should be required when ERV is given to subjects with either renal or hepatic impairment.

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1830. Phenotypic Resistance Antibiotic Resistance in ZEUS: A Multi-center, Randomized, Double-Blind Phase 2/3 Study of ZTI-01 vs. Piperacillin-Tazobactam (P-T) in the Treatment of Patients with Complicated Urinary Tract Infections (cUTI) Including Acute Pyelonephritis (AP) - Paul B Eckburg, MD1; David Skarinisky, BS2; Anita Das, PhD2 and Evelyn J. Ellis-Grosse, PhD1; Zavante Therapeutics, Inc., San Diego, California, USA; Strategic Consulting, Guerneville, California

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Background. Phenotypic resistance profiles are frequently employed to target appropriate antibiotic treatments. With increasing rates of resistance, antibiotics with novel mechanisms of action are needed. ZTI-01 (fosfomycin for injection) is an injectable epoxide antibiotic with a broad spectrum of activity including multi-drug-resistant (MDR) pathogens. ZTI-01 acts at an early step in cell wall synthesis inhibition by covalently binding to MurA, and is being developed for the treatment of complicated urinary tract infections (cUTI) and acute pyelonephritis (AP) in the US.

Methods. ZEUS study was a multicenter, randomized, double-blind Phase 2/3 trial designed to evaluate safety and efficacy of ZTI-01 in treatment of hospitalized adults with cUTI or acute pyelonephritis vs. piperacillin/tazobactam (P-T). Patients received either 6 g ZTI-01 or 4.5 g P-T as 1-hour IV infusions q8h for a fixed 7 days (up to 14 days if concurrent bacteremia). Clinical cure and microbiologic eradication were assessed at the test-of-cure (TOC) visit (Day 19). Using minimum inhibitory concentrations (MICs), blood or urine isolates bearing phenotypic resistance for extended-spectrum β-lactamases (ESBL: ≤2 µg/mL, aminoglycosides, carbapenem-resistant Enterobacteriaceae (CREE: ≥24 µg/mL imipenem or meropenem), Amino-R (gentamicin or amikacin resistance), or MDR (nonsusceptibility ≥3 classes) were identified to assess patient and microbiologic outcome.

Results. In the m-MITT population, 123/362 patients (34%) were infected with a pathogen exhibiting phenotypic resistance: MDR (19%), ESBL (31%), Amino-R (17%), and CRE (6.1%). Clinical cure and microbiologic eradication are presented in Table 1.

Table 1. Phenotypic Resistance (TOC, m-MITT, % (n))

|          | ESBL | Amino-R | CRE | MDR |
|----------|------|---------|-----|-----|
| ZTI-01   | 93%  | 55%     | 97% | 67% |
| P-T      | 93%  | 47%     | 94% | 38% |

 Disconnect. P. B. Eckburg, Zavante Therapeutics, Inc.; Consultant and Shareholder, Consulting fee; D. Skarinisky, Zavante Therapeutics, Inc.; Employee and Shareholder, Salary; A. Das, Zavante Therapeutics, Inc.; Consultant, Consulting fee; E. J. Ellis-Grosse, Zavante Therapeutics, Inc.; Employee and Shareholder, Salary.

1831. Population Pharmacokinetic and Pharmacokinetic/Pharmacodynamic Analyses of Cefiderocol in Subjects Without Infection and Patients With Complicated Urinary Tract Infection and Acute Uncomplicated Pyelonephritis - Takayuki Katsube, PhD1; Nao Kawaguchi, BSc2; Roger Echols, MD, FIDSA1 and Toshihiro Wajima, PhD1; Shionogi & Co., Ltd., Osaka, Japan, 1Shionogi, Inc., Florham Park, New Jersey

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Background. Cefiderocol (also known as S-649266) is a novel parenteral siderophore cephalosporin discovered by Shionogi & Co., Ltd., which exhibits potent efficacy against various Gram-negative bacteria including carbapenem-resistant strains. The aim of this study is to perform a population pharmacokinetic (PK) analysis based on plasma concentrations of cefiderocol in subjects without infection and patients with complicated urinary tract infection (cUTI) (without or with pyelonephritis) or acute uncomplicated pyelonephritis (AUP) caused by Gram-negative pathogens, and evaluate pharmacokinetic/pharmacodynamic (PK/PD) relationship based on fraction of time for which free drug concentration in plasma exceeds MIC over dosing interval (T₁₂₅₀).

Methods. A population PK analysis was performed using a total of 257 cefiderocol concentrations in plasma from 91 phase 1 subjects with varying renal function and 238 patients with cUTI or AUP. Covariates were explored from subjects' background data. PK/PD analyses were performed to evaluate the relationship between T₁₂₅₀ and clinical, microbiological, and composite (clinical + microbiological) responses in the patients.

Results. Plasma concentrations of cefiderocol were adequately described by the developed models. Renal function markers, body weight, and disease status (with or without infection) were significant covariates. Renal function markers were the most influential factors. The post-hoc analyses suggested that the effect of body weight on PK would not be clinically significant. Clearance and volume of distribution of cefiderocol were 26% and 36% higher in patients with infection, respectively, than those in subjects without infection. T₁₂₅₀ values were more than 75% in all patients (100% T₁₂₅₀ in most patients). The clear PK/PD relationships were not identified for any efficacy of responses. The PK/PD analysis was confounded by high urine concentrations of cefiderocol.

Conclusion. Cefiderocol PK would be predictable with renal function markers. The exposure to cefiderocol in patients with infection would be modestly lower than that in subjects without infection. A sufficient exposure to cefiderocol was provided by the tested dosages of cefiderocol in patients with cUTI or AUP.

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1832. Impact of Meal Timing on Eravacycline Exposure During the Oral Portion of an IV to Oral Transition Dosing Regimen - Patrick Horn, MD, PhD1; Susan Redican, MS2 and Larry Tsai, MD1; Tetraphase Pharmaceuticals, Watertown, Massachusetts, 1Clinical Operations, Tetraphase Pharmaceuticals, Watertown, Massachusetts

Session: 231. Clinical Study with New Antibiotics and Antifungals Saturday, October 7, 2017: 12:30 PM

Background. Eravacycline (ERV) is a novel fluorocycline being developed for the treatment of serious infections, including those caused by MDR pathogens. Multivariate analysis of data from a phase 3 study of ERV in complicated urinary