1336. Assessment of the In Vivo Efficacy of WCK 5222 (Cefepime–Zidebactam) Against Carbapenem-Resistant Acinetobacter baumannii (CR-ACBn) in the Neutropenic Murine Thigh Infection Model
Saša Almaržer-Kušan, PharmD1; Lindsey Avery, PharmD2; Kamilia Abdelraouf, PhD and David P. Nicolau, PharmD, FCCP, FIDSA. 1Department of Pharmacy, University of Jordan, Amman, Jordan; 2Department of Pharmacy, King Saud University, Saudi Arabia, 3Center of Anti-Infective Research and Development, Hartford Hospital, Hartford, Connecticut, 4Division of Infectious Diseases, Hartford Hospital, Hartford, Connecticut.

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Background. Zidebactam (ZID) is a novel β-lactam enhancer with high binding affinity to PBP2a and intrinsic activity against many Gram-negative pathogens, with the exception of ACBn. ZID also inhibits β-lactamases but not OXA carbapenemases associated with ACBn or metallo-β-lactamases. However, WCK 5222 (a combination of cefepime [FEP] and ZID) has shown in vitro activity against ACBn, including OXA producers. Moreover, we have previously shown that WCK 5222 has a prolonged regimen (HSR) that causes extensive (i.e., >2-log) eradication of ACBn from neutropenic mice. This study aimed to evaluate the in vivo efficacy of the HSR of WCK 5222 compared with FEP HSR and ZID HSR alone against ACBn in the neutropenic murine thigh infection model.

Methods. Six CR-ACBn clinical isolates, including five isolates expressing OXA-23 or OXA-24, were studied. FEP and WCK 5222 MICs were 128 to >512 and 64 mg/L, respectively. The ZID MIC was >512 mg/L for all isolates. ICR mice were rendered transiently neutropenic via cyclophosphamide prior to thigh inoculation with bacterial suspensions of 10^5 CFU/mL. Treatment mice received either FEP HSR (equivalent to a clinical dose of 2 g IV q8h as a 1 hour infusion), ZID HSR (equivalent to a clinical dose of 1 g IV q6h as 1 hour infusion), or WCK 5222 HSR (FEP HSR + ZID HSR). Control mice were vehicle-dosed. Changes in log_{10} CFU/mL at 24 hours compared with 6 hours controls were measured to assess efficacy.

Results. The average log_{10} CFU/thigh at 0 hours across all isolates was 5.85 ± 0.22. Compared with 0 hours control, the mean bacterial growth at 24 hours in the untreated control mice, FEP HSR, and ZID HSR were 2.34 ± 0.93, 1.36 ± 1.40, and 2.04 ± 0.60 log_{10} CFU/thigh, respectively. The WCK 5222 HSR produced a decline in bacterial burden for all isolates [mean reduction of -2.09 ± 1.01 log_{10} CFU/thigh]; 4/6 isolates achieved ≥2-log reduction while ≥2-log reduction was attained with the remaining two isolates.

Conclusion. HSR of WCK 5222 showed potent in vivo activity against CR-ACBn and FEP and WCK 5222 MICS in the murine thigh model, which is a pathogen, with the β-lactam enhancing effect of ZID, driven by the complementary PBP binding of FEP and ZID. These results support the clinical evaluation of WCK 5222 for the management of infections due to CR-ACBn.

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1337. SYN-004 (Ribaxamase) Protects the Gut Microbiome of Patients Treated With Ceftriaxone From Disruption and Reduces the Emergence of Antimicrobial Resistance
John Kokai-Kun, PhD1; Charles Le, PhD1; Kenneth Trout, MS2; Julia Cope, PhD3 and Joseph Sliman, MD, PhD1. 1Synthetic Biologics, Inc., Rockville, Maryland, 2Diversigen, Inc., Houston, Texas.

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Background. When β-lactam antibiotics are administered intravenously, a significant portion of each dose can be excreted through the bile into the intestine. This excess antibiotic disrupts the balance of the gut microbiome, making the recipient more susceptible to certain infections and can lead to the emergence of antimicrobial resistance. SYN-004 (ribaxamase) is an orally administered β-lactamase designed to be given with β-lactam antibiotics (penicillins and cephalosporins) to decrease excess antibiotics excreted into the upper GI tract before they can disrupt the gut microbiome and resistome.

Methods. SYN-004 (ribaxamase) was found to have a significant reduction in Clostridium difficile infection in patients receiving ceftriaxone + ribaxamase, longitudinal fecal samples were collected from the patients. DNA extracted from these samples was 16S rRNA and whole genome sequenced, and the sequences were analyzed for changes in the gut microbiome and resistome. Statistical analyses were performed to determine correlations between changes in the gut microbiome and resistome and clinical study data.

Results. Sequencing analyses revealed that ribaxamase protected the integrity of the gut microbiome, including preventing enterocolonial mono-domination (defined as 13 to 30% of the microbiome being from one genus), and identified over 1,300 AMR genes in the gut resistome. LefSe analysis of the gut resistome identified a family of β-lactamases (CIXA) and vancomycin resistance genes which demonstrated a significant increase in placebo-treated vs. ribaxamase-treated patients from pre-to post-antibiotics. Analysis by
qPCR supported both new acquisition of these genes and expansion of existing AMR pools. Further statistical analyses demonstrated significant correlations between changes in the gut resistome and clinical study parameters including β-lactamase gene frequency and study drug assignment, and efflux pump gene frequency and vancomycin resistance.

**Conclusion.** Taken together, these findings demonstrated that coadministration of rifampin with IV β-lactam antibiotics could improve the integrity of the gut microbiome and may help limit the emergence of AMR induced by these antibiotics.

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1338. A Pooled Analysis of Patients With Wound Infections in the Phase 3 REVIVE Trials: Randomized, Double-blind Studies to Evaluate the Safety and Efficacy of Iclaprim Vs. Vancomycin for Treatment of Acute Bacterial Skin and Skin Structure Infections

David Huang, MD, PhD, FIDSA, FACP; G. Ralph Corey, MD; Thomas L. Holland, MD; Thomas P. Lodise Jr., PharmD, PhD; William O’Riordan, MD; Mark Wilcox, MD; Thomas M. File Jr., MD; Matthew Dryden, MD, FRCPath, FRCPS; Antonio Torres, MD, PhD, FERS; Barbara Balser, DVM and Eve Desplats, BS;

**Motif BioSciences:** Employee, Salary.

**Amplyx Pharmaceuticals, Inc.:** Employee, Salary.

**Synthetic Biologics, Inc.:** Employee, Salary.

**Michigan, Ann Arbor, Michigan, MI**

**North Carolina, NC**

**New Jersey, NJ**

**Ohio, OH**

**Summa Health System, Akron, Ohio, OH**

**August Pi i Sunyer Biomedical Research Institute (IDIBAPS), CIBERES, Barcelona, Spain**

**Veristat, Southborough, Massachusetts**

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**Background.** The objective of this evaluation was to provide an analysis of pooled efficacy data from two parallel phase 3 trials of iclaprim, a diaphorase reductase inhibitor, compared with vancomycin for the treatment of patients with wound infections including surgical site infections (SSI).

**Methods.** A pooled analysis of patients with wound infections was conducted from two parallel Phase 3 double-blind, randomized (1:1), active-controlled, multinational, multicenter trials (REVIVE-1 and REVIVE-2), which included a total of 602 patients with wound infections. The data were analyzed separately and then pooled to determine the efficacy of iclaprim 80 mg fixed dose compared with vancomycin 15 mg/kg. Both drugs were administered intravenously every 12 hours for 5 to 14 days according to the investigator assessment of clinical response. The primary endpoint of these studies was to determine whether iclaprim was noninferior (NI; 10% margin) to vancomycin with wound infections. These results suggest that iclaprim may be a valuable treatment option for patients with wound infections (see table). The median treatment duration for both iclaprim and vancomycin was 7 days (range 5–14 days).

**Conclusion.** In this post-hoc analysis of the REVIVE studies, iclaprim achieved NI to vancomycin in both studies, based on ETP at ET in the subgroup of patients with wound infections. These results suggest that iclaprim may be a valuable treatment option for patients with wound infections, including SSIs, suggested or confirmed to be due to Gram-positive pathogens.

**Disclosures.** D. Huang, Motif BioSciences: Employee, Salary. G. R. Corey, Motif BioSciences: Board Member, Consulting fee. T. L. Holland, Basilea: Consultant, Consulting fee. T. P. Lodise Jr., Motif BioSciences: Board Member, Consulting fee. W. O’Riordan, Motif BioSciences: Board Member, Consulting fee. M. Wilcox, Motif BioSciences: Board Member, Consulting fee. T. M. File Jr., Motif BioSciences: Board Member, Consulting fee. W. O’Riordan, Motif BioSciences: Board Member, Consulting fee. M. Wilcox, Motif BioSciences: Board Member, Consulting fee. T. M. File Jr., Motif BioSciences: Board Member, Consulting fee. W. O’Riordan, Motif BioSciences: Board Member, Consulting fee. M. Wilcox, Motif BioSciences: Board Member, Consulting fee. T. M. File Jr., Motif BioSciences: Board Member, Consulting fee. W. O’Riordan, Motif BioSciences: Board Member, Consulting fee. M. Wilcox, Motif BioSciences: Board Member, Consulting fee. T. M. File Jr., Motif BioSciences: Board Member, Consulting fee. W. O’Riordan, Motif BioSciences: Board Member, Consulting fee. M. Wilcox, Motif BioSciences: Board Member, Consulting fee. T. M. File Jr., Motif BioSciences: Board Member, Consulting fee. W. O’Riordan, Motif BioSciences: Board Member, Consulting fee. M. Wilcox, Motif BioSciences: Board Member, Consulting fee.