696. Cefiderocol Susceptibility Against Molecularly Characterized Carbapenemase-Producing Gram-Negative Bacteria in North America and Europe Between 2014 and 2017: SIDERO-WT-2014 to -2016 Studies Takafumi Sato, PhD; Masakatsu Tsuji, PhD; Krystyna M. Kazmierczak, PhD; Meredith M. Hackel, PhD; Roger Echols, MD; Yoshinori Yamano, PhD; Daniel F. Sahm, PhD, D(ABMM), FAAAM; 1 Sionogoi Inc., Osaka, Japan; 2 Sionogoi Co., Ltd., Osaka, Japan; 3 International Health Management Associates, Inc., Schaumberg, Illinois; 4 Infectious Disease Drug Development Consulting LLC, Easton, Connecticut Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs Thursday, October 3, 2019: 12:15 PM Background. Antibiotic susceptibility surveillance is the foundation for selecting treatment options as well as immediate and long-term strategies for combating antimicrobial resistance. We have conducted three surveillance studies SIDERO-WT-2014/2015/2016 with approximately 30,000 Gram-negative strains isolated in North America and Europe between 2014 and 2017. Here, we present the latest data of molecular analysis on acquired carbapenemase genes and antibiotic susceptibility of 3696 meropenem-nonsusceptible strains in the surveillance studies.

Methods. Meropenem-nonsusceptible strains isolated in North America (n = 1063) and Europe (n = 2682), consisting of 1897 Acinetobacter baumannii, 1154 Pseudomonas aeruginosa, 447 Klebsiella pneumoniae, and 193 other Enterobacteriaceae were tested. Conventional PCR was used to detect known carbapenemases. Cefiderocol MICs were determined by broth microdilution method using iron-depleted cation-adjusted Mueller–Hinton broth.

Results. The percentages of known carbapenemases detected in 3 main pathogens are shown in the Table. In A. baumannii complex, OXA-23 was predominatly followed by OXA-24 in most countries. The detection rates of VIM in P. aeruginosa were 240% in Greece and Russia, but none of the strains in the United States carried VIM. In K. pneumoniae, the predominant carbapenemase varied among the countries, with KPC predominating in the USA, Greece and Italy, while OXA-48-like was dominant in Russia, Spain and Turkey. Cefiderocol MICs were ≤4/≤4 μg/mL against these 3 pathogens in all 6 countries, except for A. baumannii strains in Russia.

Conclusion. Carbapenemase detection rates, especially in P. aeruginosa and K. pneumoniae, were quite different among the countries. Cefiderocol demonstrated potent in vitro activity against meropenem-nonsusceptible strains irrespective of the presence of specific carbapenemases.

Disclosures. All authors: No reported disclosures.

697. Evaluation of Contezolid Activity to Anaerobic and Gram-positive cocci Isolates from a Phase 3 Acute Bacterial Skin and Skin Structure Infection Clinical Trial (MRX-1-06) Yang Yang, Master of medicine1,2; Fupin Hu, PhD1; Demei Zhu, Bachelor2; 1 Institute of Antibiotics, Huashan Hospital, Fudan University, Shanghai, China (People’s Republic), 2 Key Laboratory of Clinical Pharmacology of Antibiotics, National Health and Family Planning Commission, Shanghai, China (People’s Republic) Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs Thursday, October 3, 2019: 12:15 PM Background. Contezolid (MRX-I) is an oxazolidinone in development for the treatment of acute bacterial skin and skin structure infections (ABSSSI). In this study, in vitro susceptibility (S) for Contezolid and comparator agents for Gram-positive (GP) and anaerobic isolates from Phase 3 ABSSSI clinical trials were determined.

Methods. 313 isolates were collected from 65 participating sites and sent to a central laboratory for MIC testing. Clinical isolates included 34 anaerobes (15 Fusobacteria magna, 8 Actinomyces spp., 4 Prevotella spp., 3 Propionibacterium avidum, 2 Peptostreptococcus spp., 1 Veillonella spp., and 1 Bacteroides fragilis), 187 S. aureus (59. 7%), 12 S. pyogenes, 5 Enterococcus and 75 other Gram-positive organisms. Broth micro-dilution method was used to determine the MIC of contezolid, linezolid and other comparators to facultative isolates. Agar dilution was carried out for the anaerobes.

Results. For both 33 MRSA and 154 MSSA MIC<50 values of contezolid and linezolid were 2 mg/L. One E. faecalis showed decreased susceptibility to oxazolidinones (both MIC = 4). 1 mg/L contezolid and linezolid could inhibit 12 S. pyogenes. 2 mg/L contezolid and linezolid could inhibit 15 F. magna. 0.5 mg/L contezolid and linezolid could inhibit 8 Actinomyces spp. To one Bacteroides fragilis, two Prevotella bivia and one Leuconostoc lactis (Intrinsic resistant to vancomycin) the MIC of contezolid were 4 or 8 mg/L. In general, Contezolid had lower or equal MIC<50 values against both GP and ANA species compared with linezolid for all organisms.

Conclusion. Contezolid demonstrated potent in vitro antibacterial activity against Gram-positive and anaerobic isolates tested. These data suggest that contezolid might be a beneficial supplement to the arena against MDR Gram-positive infection.

Disclosures. All authors: No reported disclosures.

698. In vitro Activity of a New Generation Oxazolpyrazole Antibiotic Against Multidrug-Resistant Gram-Negative Bacilli Joel Goldberg, MD, PhD; Christopher Bethel, MS; Kristine M. Huier, BS; Kristina M. Papp-Wallace, PhD; Federico Perez, MD, MS; Elizabeth Spencer, MS; Denton Hoyer, PhD; Mark Plummer, PhD; Robert A. Bonomo, MD; 1 Case Western Reserve University, Cleveland, Ohio; 2 Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio; 3 Louis Stokes VA Medical Center, Cleveland, Ohio; 4 Louis Stokes Cleveland VAMC and Case Western Reserve University, Cleveland, Ohio; 5 Yale University, West Haven, Connecticut; 6 Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio Session: 68. Novel Antimicrobials and Approaches Against Resistant Bugs Thursday, October 3, 2019: 12:15 PM Background. Multidrug-resistant Gram-negative bacilli (MDRGNB) are emerging as a challenging cause of hospital-acquired infections and represent a critical need for innovative antibacterial development. New oxazolpyrazole agents targeting penicillin-binding proteins (PBPs) based on a non-β-lactam core and incorporating a siderophore moiety (Figure 1) which facilitates transport to the periplasm are being developed that show promise against Gram-negative organisms including multidrug-resistant strains of E. coli, K. pneumoniae and P. aeruginosa.

Methods. YU253434, an example of this new class of antibacterials, was investigated in vitro. Minimum inhibitory concentrations (MICs) were determined by broth microdilution against a representative panel comprising 15 strains each of E. coli, K. pneumoniae and P. aeruginosa, which contain extended-spectrum β-lactamase (ESBL) and/or carbapenemases genes. All studies were performed according to current Clinical & Laboratory Standards Institute (CLSI) guidelines using iron-depleted media. Cefazidime breakpoints were arbitrariness chosen as a reference for YU253434 (susceptibilities ≤4 μg/mL for Enterobacteriaceae and ≤8 μg/mL for P. aeruginosa).

Results. MIC testing (Figures 2–4) against E. coli showed 11 strains were YU253434 susceptible (compared with 6 for cefazidime, and 3 for imipenem); against K. pneumoniae 13 strains were YU253434 susceptible (compared with 2 for cefazidime and 6 for imipenem); against P. aeruginosa 10 strains were YU253434 susceptible (compared with 0 for both cefazidime and imipenem). There appeared to be no correlation between YU253434 resistance and the presence of specific lactamase genes.

Conclusion. YU253434, a new generation oxazolpyrazole antibiotic, demonstrated promising in vitro potency against a panel of E. coli, K. pneumoniae, and P. aeruginosa strains which contain ESBL and/or carbapenemases.
Disclosures. All authors: No reported disclosures.

699. Hepatobiliary Safety in Adults With Community-Acquired Bacterial Pneumonia (CABP) Treated With Lefamulin (LEF) or Moxifloxacin (MOX): Pooled Analysis of Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Study Results

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Background. LEF efficacy and safety were shown in 2 noninferiority trials (LEAP 1/2) vs. MOX in adults with CABP. We assessed the hepatobiliary safety of LEF based on pooled analyses of LEAP 1/2 data.

Methods. In LEAP 1, PORT III–V patients received LEF 150 mg IV q12h for 5–7 days or MOX 400 mg IV q24h for 7 days, with optional IV-to-oral switch (600 mg LEF q12h or 400 mg MOX q24h). In LEAP 2, PORT II–IV patients received oral LEF 600 mg q12h for 5 days or oral MOX 400 mg q24h for 7 days. Exclusion criteria included infection with HBV/HCV, acute hepatitis, cirrhosis, AST or ALT >5xULN, total bilirubin >1.5xULN (unless Gilbert’s disease), AST or ALT >3xULN and total bilirubin >2xULN, and manifestation of end-stage liver disease. Hepatic safety was assessed from baseline (BL) and multiple post-BL blood samples using a central laboratory, TEAEs, and expert consultant adjudication. Pooled analyses included all randomized/treated patients (safety population).

Results. Of 1282 randomized/treated patients, 1251 had BL and post-BL hepatobiliary data (table). Post-BL distribution of ALT/AST was generally similar for both groups, although ALT >AST in the absence of muscle injury or alcohol use. Overall, rates of patients experiencing an increase in ALT/AST >3xULN, ALP >2xULN, or total bilirubin >1.5xULN were low (table). Patients with elevated vs. normal BL transaminases (TAs) were more likely to have post-BL elevations >3xULN, but the vast majority remained <5xULN. Among patients with ALT >5xULN, peak increases were generally seen in the first week after the first LEF dose and declined to within/near normal levels by late follow-up (day 28); for MOX, time to peak ALT was less consistent (figure). No LEF pt and 1 MOX pt met laboratory criteria for Hy’s Law. Elevations in TAs were reversible, with no evidence of chronic injury. The LEF injury pattern was predominantly hepatocellular (50.0%/mixed 40.0%), with no apparent gender, age, or ethnic predominance. TEAEs in the hepatobiliary disorders system organ class were reported in 6 (0.9%) LEF patients and 6 (0.9%) MOX patients, with similar levels seen in patients with elevated BL TAs. There were no symptomatic patients, severe disease, or evidence of hypersensitivity.

Conclusion. Low incidences of hepatobiliary parameter elevations and TEAEs were observed, with no apparent differences between LEF and MOX.

Table. Maximum Postbaseline Increases in Hepatobiliary Parameters

| Parameter          | LEAP 1 (n=280) | MOX (n=287) | LEAP 2 (n=355) | MOX (n=361) | Pool (n=632) |
|--------------------|----------------|-------------|----------------|-------------|--------------|
| ALT >3xULN         | 19 (7.1)       | 17 (6.4)    | 15 (4.2)       | 17 (4.7)    | 34 (5.5)     |
| ALT >5xULN         | 6 (2.2)        | 5 (1.8)     | 7 (2.0)        | 3 (0.8)     | 13 (2.1)     |
| AST >10xULN        | 1 (0.4)        | 0           | 1 (0.3)        | 0           | 2 (0.3)      |
| AST >3xULN         | 11 (4.1)       | 7 (2.6)     | 12 (3.4)       | 8 (2.2)     | 23 (3.7)     |
| AST >5xULN         | 2 (0.7)        | 2 (0.7)     | 6 (1.7)        | 5 (1.4)     | 8 (1.3)      |
| ASAT >10xULN       | 1 (0.4)        | 0           | 1 (0.3)        | 0           | 2 (0.3)      |
| ALP >2xULN         | 5 (1.9)        | 5 (1.9)     | 14 (3.9)       | 6 (1.7)     | 19 (3.0)     |
| Total bilirubin >1.5xULN | 3 (1.1) | 3 (1.1) | 3 (0.8) | 3 (0.8) | 6 (1.0) |
| Total bilirubin >2xULN | 0            | 2 (0.7)     | 2 (0.6)        | 0           | 2 (0.3)      |

AL: aspartate aminotransferase; ALT: alanine aminotransferase; ASAT: aspartate aminotransferase; LEF: lefamulin; MOX: moxifloxacin; ULN: upper limit of normal.

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700. Safety and Efficacy of Omadacycline in Patients With Diabetes in Phase 3 Clinical Studies

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Background. The risk of serious infections and poor treatment outcomes is reported to be higher in patients with diabetes compared with the general population. Omadacycline (OMC) is an intravenous (IV) and oral aminomethylcycline antibiotic approved in the US to treat acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP) in adults. Here we assessed safety and efficacy results from OMC Phase 3 studies (ABS331: Omadacycline in Acute Skin and skin structure Infections Study [OASIS]-1 and OASIS-2; CABP: Omadacycline for Pneumonia Treatment In the Community study [OPTIC]), by diabetes history.

Methods. In OASIS-1 (IV to optional oral medication) and OASIS-2 (oral only), patients were randomized to OMC or linezolid (LZD) for 7–14 days. In OPTIC, patients were randomized to IV OMC or moxifloxacin (MOX) for 7–14 days, with optional transition to oral medication. Data from OASIS-1 and OASIS-2 were pooled, and patient...