therapeutic options include combinations of aztreonam (ATM), which is resistant to hydrolysis by MBLs, plus ceftazidime/avibactam (CZA) or meropenem/vaborbactam (M/V) for coverage of relevant SBLs. However, these selections add a level of complexity to clinical management compared with administration of a single antibiotic as monotherapy.

Methods. Minimum inhibitory concentrations (MICs) of WCK 5222 (ceposefine/zonebactam), ATM, CZA, and M/V were determined with Liofilchem MIC Test Strips against SBL- and MBL-positive CRE (N = 15). The gradient diffusion strip (GDS) cross method was used to assess the activities of CZA+ATM and M/V+ATM. Additive interactions as defined by fractional inhibitory concentration indices ≤ 1 would be predicted based upon the known genotypic profiles; thus, the relative activities of the combination regimens were compared with the “zone of hope” (ZOH) test. The size of the ZOH (the zone of inhibited growth) was quantitated by multiplying the observed length of inhibited growth (in mm) adjacent to each GDS from the point of intersection. The Mann–Whitney rank-sum test was used to assess differences.

Results. All isolates (N = 15) contained one MBL and ≥2 SBLs, and were resis-
tant to ATM, CZA, and M/V with the exception of one isolate intermediate to M/V (MIC = 8 μg/mL). The WCK 5222 MIC50 (range) was 1 (0.19–2) μg/mL. The median (inter-
quartile range) ZOH product for CZA+ATM and M/V+ATM was 75.4 (62.8–93.7) and 23.5 (14.1–60.4), respectively (P = 0.002). In strains that produced OXA-type carbapen-
emases (n = 6), the median ZOH product for CZA+ATM and M/V+ATM was 78.1 and 23.2 (n = 6, respectively), respectively (P = 0.052).

Conclusion. WCK 5222 displayed potent in vitro activity against SBL- and MBL-
positive CRE, warranting further pre-clinical in vitro evaluation, as a new therapy option. When considering the co-expression of SBL and MBL, CZA+ATM appears to offer enhanced coverage compared with M/V+ATM.

Disclosures. All authors: No reported disclosures.

686. 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)

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Background. Contezolid (MRX-1) is an oxazolidinone in development for the treatment of acute bacterial skin and skin structure infections (ABSSSIs). 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 participated sites and sent to a central laboratory for MIC testing. Clinical isolates included 34 anaerobic isolates (15 Finegoldia 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 microdilution was used to determine MIC of comparator and other comparators to facultative isolates. agar dilution was carried out for the anaerobes.

Results. For both 33 MRSAs and 154 MSSA MIC50 values of contezolid and lin-
exoloid were 2 μg/L. One E. faecalis showed decreased susceptibility to oxazolidinones (both MIC = 4). 1 mg/L contezolid and linexoloid could inhibit 12 S. pyogenes. 2 mg/L contezolid and linexoloid could inhibit 15 Finegoldia magna. 0.5 μg/mL contezolid and linexoloid could inhibit 8 Actinomyces spp. To one Bacteroides fragilis, two Prevotella bivia Leuconostoc lactis (Intrinsic resistant to vancomycin) the MIC of con-
tezolid were 4 or 8 μg/mL. In general, Contezolid had lower or equal MIC50 values against both GP and ANA species compared with linexoloid for all organisms.

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

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687. In vitro Activity of a New Generation Oxypiroxazole Antibiotic Against Acinetobacter spp.

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Background. Acinetobacter spp. resistant to common antibiotics has become a worrying cause of hospital-acquired infections and represent a critical need for innova-
tive and effective new therapy developments. New copy wars are ongoing targeting agents including proteins (PBPs) based on a non-β-lactam core and incorporating a siderophore moiety (figure) which facilitates transport to the periplasm being developed which show promise against Gram-negative organisms including Acinetobacter spp.

Methods. YU253911, an example of this new class of antibacterials, was char-
acterized in vitro. Minimum inhibitory concentrations (MICs) were determined by broth microdilution against a collection of 200 previously described (whole-genome sequencing) Acinetobacter isolates including 98 carbapenem-resistant A. baumannii strains. YU253911 antimicrobial activity was also evaluated in combination with complementary PBP agents and β-lactamase inhibitors by MIC and disc diffusion testing. All studies were performed according to current Clinical and Laboratory Standards Institute (CLSI) guidelines using iron-depleted media. Breakpoints for cef-
tazidime were arbitrarily chosen as reference.

Results. Using cefotaxime (breakpoint 68 μg/mL) as a comparator, 175 of the 200 Acinetobacter isolates were susceptible to YU253911, which possessed an MIC50 of 3.5 μg/mL and an MIC90 of 16 μg/mL. This compared favorably to all previously tested β-lactams including penicillins, cephalosporins, monobactams and carbapenems (MIC90 > 16 μg/mL). Against the subset of carbapenem-resistant A. baumannii isolates, YU253911 potency was similar with an MIC50 of 1 μg/mL. Genetic analysis showed β-lactamase genes, including OXA-23 and other carbapenemases, were com-
mon in both YU253911-resistant and susceptible strains.

Conclusion. YU253911 demonstrates promising in vitro potency against a collection of Acinetobacter isolates and compares favorably to β-lactam antibiot-
ics. Understanding interactions with PBP agents and β-lactamase inhibitors is being explored as well as further studies on the mechanism of resistance.

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688. In Vitro Activity of Eravacycline, a New Tetracycline Analog, and Comparators Against the Six Most Commonly Isolated Ribotypes of Clostridioides difficile

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Background. Eravacycline is a novel, tetracycline class antibacterial indicated for the treatment of complicated intra-abdominal infections in adults. In clinical trials, patients given eravacycline had a low likelihood of developing Clostridioides difficile infection (CDI). We hypothesized this was likely due, in part, to the in vitro susceptibility of eravacy-
cline to C. difficile. The purpose of this study was to test the in vitro susceptibility of eravacy-
cline vs. comparators on contemporary clinical isolates representing common ribotypes, including isolates with decreased susceptibility to metronidazole and vancomycin.

Methods. Two hundred and thirty-four isolates from our biobank were selected from the six most common ribotypes (F001, F002, F014-020, F027, F106, and F255). Minimum inhibitory concentrations (MIC) at 24 hours were measured according to CLSI guidelines for eravacycline, vancomycin, metronidazole and fidaxomicin. MICs were tabulated and are presented as the geometric mean by ribotype.

Results. Geometric MIC results are shown in Table 1. Eravacycline was the most potent antibacterial tested followed by fidaxomicin, metronidazole, and vancomycin. Results were consistent amongst all ribotypes, including isolates with reduced suscepti-
Bility to vancomycin and metronidazole.

Conclusion. Eravacycline displayed potent in vitro activity against a large collec-
tion of clinical C. difficile isolates. These data provide insight into why patients given eravacycline had a low likelihood of developing CDI and support further research to bet-
ter understand the use of eravacycline to prevent or potentially treat patients with CDI.

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