1207. Analysis of Oritavancin Activity against Gram-Positive Clinical Isolates Responsible for Bacterial Endocarditis in United States and European Hospitals (2008–2016)

Michael A. Pfaller, MD; Helio S. Sader, MD; Dee Shortridge, PhD; Robert K. Flamm, PhD and Rodrigo E. Mendes, PhD; JMI Laboratories, Inc., North Liberty, Iowa

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing

Background. Oritavancin (ORI) has demonstrated potent activity against CA-RTI pathogens, including SPN, HI, and MC. These data supported the continued study of ORI as a potential treatment for community-acquired pneumonia.

Disclosures. D. Shortridge, Melinta Therapeutics: Research Contractor, Research grant; J. M. Streit, Melinta Therapeutics: Research Contractor, Research grant; M. D. Huband, Melinta Therapeutics: Research Contractor, Research grant; P. R. Rhomberg, Melinta Therapeutics: Research Contractor, Research grant; R. K. Flamm, Melinta Therapeutics: Research Contractor, Research grant

1209. In Vitro Activity of Evacrylavine and Comparator Antimicrobials Against 143 Strains of Bacteroides Species

Diane Citron, B.Sc.; J. Kern Tyrrell, B.Sc.; and E. Goldstein, MD; *R.M. Alden Research Labs, Culver City, California, †R.M. Alden Research Labs, Santa Monica, California

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing

Background. Evacrylavine (ERV) is the first fully synthetic fluorocycline with activity against tetracycline (TET)-resistant organisms. In addition, it is 2–8 times more potent than tigecycline (TGC). Like other tetracyclines, it inhibits protein synthesis by binding to the 30S ribosomal subunit exhibiting a broad spectrum of activity.

Disclosures. D. Shortridge, The Medicines Company: Research Contractor, Research grant; R. K. Flamm, The Medicines Company: Research Contractor, Research grant; R. E. Mendes, The Medicines Company: Research Contractor, Research grant

1208. In Vitro Evaluation of Delafloxacin Activity when Tested Against Contemporaneous Community-Acquired Bacterial Respiratory Tract Infection Isolates (2014–2016): Results from the SENTRY Antimicrobial Surveillance Program

Dee Shortridge, PhD; Jennifer M. Streit, BS; Michael D. Huband, BS; Paul Rhomberg, BS and Robert K. Flamm, PhD; JMI Laboratories, Inc., North Liberty, Iowa

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing

Background. Delafloxacin (DLX) is a broad-spectrum fluoroquinolone (FQ) antibiotic that has completed clinical development (oral and intravenous formulations) with the new drug application currently under the Food and Drug Administration review for the treatment of acute bacterial skin and skin structure infections (ABSSSI). DLX is also in clinical trials for community-acquired bacterial pneumonia. In this study, in vitro susceptibility results for DLX and comparator agents were determined for clinical isolates from community-acquired respiratory tract infections (CA-RTI) collected in medical centers in the United States and Europe participating in the SENTRY surveillance program during 2014–2016.

Disclosures. A total of 3,093 isolates that included 1,673 Streptococcus pneumoniae (SPN), 805 Haemophilus influenzae (HI) and 555 Moraxella catarrhalis (MC) were collected during 2014–2016 and included only 1 isolate/patient/infection episode. Isolate identifications were confirmed at JMI Laboratories. Susceptibility testing was performed according to CLSI reference broth microdilution methodology, and results were interpreted per CLSI (2017) breakpoints. Other antibacterials tested included levofloxacin (LVX) and penicillin. B-lactamase production for HI and MC was determined by the nitrocephin disk test.

Results. DLX demonstrated potent in vitro activity against SPN (MIC: 0.015/0.03 µg/mL). Activity remained the same for penicillin-intermediate or -resistant isolates. For 23 LVX nonsusceptible SPN, the DLX MIC ranged from 0.125–2 mg/L with all isolates having DLX MIC values ≤1 mg/L. For HI, the DLX MIC was ≤0.001/0.004 mg/L, and for MC the MICs were 0.008–0.03 mg/L. DLX activity was unaffected by the presence of B-lactamase for either HI or MC. Activity of DLX was similar for US and European isolates.

Conclusion. Delafloxacin demonstrated potent in vitro antibacterial activity against CA-RTI pathogens, including SPN, HI, and MC. These data support the continued study of DLX as a potential treatment for community-acquired pneumonia.

Disclosures. D. Shortridge, Melinta Therapeutics: Research Contractor, Research grant; J. M. Streit, Melinta Therapeutics: Research Contractor, Research grant; M. D. Huband, Melinta Therapeutics: Research Contractor, Research grant; P. R. Rhomberg, Melinta Therapeutics: Research Contractor, Research grant; R. K. Flamm, Melinta Therapeutics: Research Contractor, Research grant

Poster Abstracts • OFID 2017:4 (Suppl 1) • 5369
Results. EO\textsuperscript{s} oregano, thyme, cinnamon bark, and lemongrass had the largest zones of inhibition against Gram-positive organisms and were larger than those of vancomycin for MRSA/MSSA. Cinnamon bark had the largest zone of inhibition against P. aeruginosa and was larger than that of meropenem. Oregano, thyme, cinnamon bark had the largest zones of inhibition against Enterobacteriaceae and were larger than those of meropenem against K. pneumoniae and E. cloacae.

Table 1. Median Zone Diameters (mm for Essential Oils)

| Isolates | Oregano | Thyme | Cinnamon | Bark | Lemon | grass | Manuka | Clove | Tea | Thieves' | Thieves' | Vancio | Marco |
|---------|---------|-------|---------|------|-------|------|-------|------|-----|---------|---------|--------|-------|
| MRSA n = 10 | 23 | 26 | 30 | 30 | 13 | 13 | 9 | 18 | 18 | ND |
| MSSA n = 10 | 26 | 30 | 29 | 30 | 18 | 15 | 8.5 | 19 | 19 | ND |
| E. coli | 90 | 70 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 |

ND=not done

Conclusion. Essential oils showed significant in vitro activity against clinical isolates, including CRE. Further study of the clinical activity of essential oils is warranted.

Disclosures. J. E. Patterson, Young Living Essential Oils: Independent Contractor, Salary

1212. Lysin CF-301 Demonstrates In Vitro Synergy with Conventional Antibiotics against Staphylococcus aureus

Karen Saue, BS\textsuperscript{a}; Alena Jandourek, MD\textsuperscript{b}; Carin Cassino, MD\textsuperscript{c} and Raymond Schuch, PhD\textsuperscript{d}; ContraFect Corp, Yonkers, New York, \textsuperscript{e}ContraFect Corp, Yonkers, New York

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing

Friday, October 6, 2017: 12:30 PM

Background. CF-301 is a novel, recombinantly-produced bacteriophage-derived lysin (cell wall hydrolase) and is the first agent of this class to enter clinical development in the US for the treatment of bacteremia including endocarditis due to S. aureus. This study evaluated the in vitro activity of CF-301 combined with each of 7 anti-staphylococcal antibiotics including those considered to be current standard of care treatments for S. aureus bacteremia (daptomycin, vancomycin, oxacillin, nafcillin, and ceftaroline) as well as linezolid and tetracycline.

Methods. MICs for CF-301 were determined using a new AST medium for broth microdilution recently endorsed by the CLSI for use with CF-301. The testing medium consisted of cation-adjusted MHB supplemented with 25% horse serum and 0.5 mM DTT. Synergy was determined by checkerboard microdilution using the fractional inhibitory concentration index (FICI) for each combination in triplicate. For each antibiopic tested, an FIC mean was derived from each set of checkerboards by averaging 3 consecutive FIC values along the growth/no growth interface for each plate. Thus, 9 values were used, to generate the final mean. Synergy was defined as an FICI of ≤0.5; indifference was >0.5 to <2, and antagonism was ≥2. Each combination was examined against 10 MSSA and 10 MRSA strains.

Results. CF-301 synergized with daptomycin and vancomycin against each MSSA and MRSA strain, with FICI values between 0.254 and 0.5. Synergy was similarly observed against all 20 strains tested with oxacillin and nalidixic acid (FICI = 0.25–0.5); for the third β-lactam, ceftaroline, synergy was observed with 17 strains (FICI = 0.75, for the remaining 3 strains). CF-301 synergized with televancin against 70% of the strains (FICI = 0.375–0.5), and was indifferent with the remainder (FICI = 0.625–1). CF-301 synergized with linezolid against 55% of the strains (FICI = 0.375–0.5), and was indifferent with the remainder (FICI = 0.625–0.75).

Conclusion. The broadly synergistic activity of CF-301 with conventional anti-staphylococcal antibiotics against MSSA and MRSA suggests that CF-301 may afford therapeutic benefit by potentiating the activity antibiotics to treat serious infections for which there is an unmet medical need to improve outcomes.

Disclosures. K. Saue, ContraFect Corp: Employee, Salary; A. Jandourek, ContraFect Corp: Employee, Salary; C. Cassino, ContraFect Corp: Employee, Salary; B. Schuch, ContraFect Corp: Employee, Salary

1213. Activity of Antistaphylococcal Lysin CF-301 against Contemporary Staphylococcus aureus Clinical Isolates from the USA and Europe

Jun Oh, PhD\textsuperscript{a}; Maria Traczewski, BS\textsuperscript{b} and Raymond Schuch, PhD\textsuperscript{d}; Microbiology, ContraFect Corp, Yonkers, New York, \textsuperscript{c}Clinical Microbiology Institute, Wilsonville, OR, \textsuperscript{d}ContraFect Corp, Yonkers, New York

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing

Friday, October 6, 2017: 12:30 PM

Background. CF-301 is a novel, recombinantly-produced bacteriophage-derived lysin (cell wall hydrolase) and is the first agent of this class to enter clinical development for the treatment of bacteremia including endocarditis due to S. aureus. This includes features of CF-301 which include rapid and pathogen-specific bactericidal activity, synergy with antibiotics, biofilm-disrupting activity, a low propensity for resistance, and the capacity to suppress antibiotic resistance. This is the first report of an international surveillance study for CF-301.

Disclosures. K. Saue, ContraFect Corp, Yonkers, New York

1211. In vitro Susceptibility Testing of Essential Oils against Gram-positive and Gram-negative Clinical Isolates, including Carbapenem-resistant Enterobacteriaceae (CRE)

Jan E. Patterson, MD, MS, FIDSA, FSHEA\textsuperscript{a}; M.L. McElmeel, BS, MT(ASCP)\textsuperscript{b} and Nathan F. Wiederhold, PharmD\textsuperscript{c}; Medicine/Infectious Diseases, UT Health San Antonio School of Medicine, San Antonio, TX; UT Health San Antonio, TX, UT Health San Antonio School of Medicine, San Antonio, Texas, UT Health San Antonio, San Antonio, Texas

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing

Friday, October 6, 2017: 12:30 PM

Background. In the era of antibiotic resistance, alternative anti-infectives must be explored. The National Action Plan for Combating Antibiotic-Resistant Bacteria calls for developing nontraditional therapeutics, including natural compounds such as essential oils (EOs). A pilot study previously showed in vitro activity of EOs against CRE and warranted further study of their antibacterial activity. We studied cinnamon bark, clove, lavender, lemongrass, eucalyptus, oregano, rosemary, thyme, tea tree, manuka, and ‘Thieves’ blend (Young Living Essential Oils, Lehi UT) against an expanded panel of Gram-positive and Gram-negative isolates.

Methods. 30 Gram-positive and 70 Gram-negative clinical isolates, including CRE, were tested using CLSI methods. Isolates were grown overnight on TSA; 0.5 McFarland suspensions in sterile water were swabbed over Mueller–Hinton agar using the Kirby–Bauer method. 20 µl of full-strength oils were pipetted onto blank paper discs placed aseptically onto the plates immediately after inoculating disks. Vancomycin was tested with Gram-positives and meropenem with Gram-negatives. Median zone diameters are shown.

Disclosures. R. E. Mendes, Merck: Research Contractor, Research grant; D. Shortridge, Merck: Research Contractor, Research grant; H. S. Sader, Merck: Research Contractor, Research grant; L. R. Duncan, Merck: Research Contractor, Research grant; R. K. Flamm, Merck: Research Contractor, Research grant

1120. Broad In Vitro Activity Analysis of Tedizolid Compared with Other Agents against a Global Collection of Gram Positive Isolates Causing Bloodstream Infections (2014-2016)

Rodrigo E. Mendes, PhD; Dee Shortridge, PhD; Helio S. Sader, MD, PhD; Leonard R. Duncan, PhD and Robert K. Flamm, PhD; JMI Laboratories, Inc., North Liberty, Iowa

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing

Friday, October 6, 2017: 12:30 PM

Background. Tedizolid (TZD) is an oxazolidinone derivative with oral and intravenous formulations approved for the treatment of acute bacterial skin and skin structure infections in the US, European countries, and other regions. This study evaluated TZD’s and comparators’ activity against a collection of clinical isolates causing bloodstream infections (BSI).

Methods. A total of 7,284 gram-positive isolates collected during the Surveillance of Tedizolid Activity and Resistance (STAR) Program for 2014–2016 were included. Bacteria were identified by standard algorithms and MALDI-TOF-MS. Susceptibility (S) testing was performed by CLSI methods, and interpretation used CLSI and EUCAST criteria.

Results. This Staphylococcus aureus collection contained 33.8% methicillin-resistant isolates. TZD was the most potent agent tested against all S. aureus (MIC\textsubscript{90} 0.12/0.12 µg/mL; 100.0% S) and the MRSA subset (Table). Other tested agents described in Table also had in vitro MSSA coverage. 15.6% of enterococci were vancomycin resistant, which were mostly Enterococcus faecium (59.8%). Linezolid (LZD), ampicillin, daptomycin (DAP), and vancomycin (VAN) showed equivalent MIC\textsubscript{90} values (1 µg/mL) against E. faecalis, but these MIC\textsubscript{90} results were 8-fold higher than TZD (MIC\textsubscript{90} 12.5 µg/mL). Although LZD and DAP were highly active (98.9–99.4%) against E. faecium, MIC\textsubscript{90} results were 16-fold lower than LZD. LZD and DAP showed the lowest MIC\textsubscript{90} values against Streptococcus pneumoniae, whereas TZD and VAN were similarly active. TZD and CPT showed the lowest MIC\textsubscript{90} values against viridans group streptococci, while CPT, ceftriaxone, and penicillin had the lowest MIC\textsubscript{90} results against β-hemolytic streptococci.

Conclusion. TZD had potent activities against this global population of gram-positive clinical isolates that caused BSI. This in vitro potency and a favorable pharmacodynamic profile may suggest TZD is a promising candidate for treating BSI in patients infected with these organisms.