1210. 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; R. Duncan, PhD and Robert K. Flamm, PhD; JMI Laboratories, Inc., North Liberty, Iowa

Session: 147. Expanded Spectrum – New Antimicrobial Susceptibility Testing
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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<sub>90</sub> 0.12/0.12 µg/mL; 100.0%) and the MRSA subset (Table). Other tested agents described in Table also had in vitro MRSA 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<sub>90</sub> values (1 µg/mL) against E. faecalis, but these MIC<sub>90</sub> results were 8-fold higher than TZD’s MIC<sub>90</sub> results. Although LZD and DAP were highly active (98.9–99.4%) against enterococci, MIC<sub>90</sub> values were 8–16-fold lower that LZD and DAP. CF-301 showed the lowest MIC<sub>90</sub> values against Streptococcus pneumoniae, whereas TZD and VAN were similarly active. TZD and CPT showed the lowest MIC<sub>90</sub> values against vanidans group streptococci, while CPT, cetaxalone, and penicillin had the lowest MIC<sub>90</sub> 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 caused by gram-positive isolates, especially E. faecium.

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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; M.L. McElmeel, BS, MT(ASCP) and Nathan P. Wiederhold, PharmD; JMI Laboratories, Inc., North Liberty, Iowa

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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) (Goal 4.4). 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 disks 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.

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

Karen Saue, BS; Alena Jandourek, MD; Cara Cassino, MD and Raymond Schuch, PhD; ContraFect Corp, New York, New York

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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 ceftazidime) as well as linezolid and televancin.

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 anti-biotic tested, an FICI was derived from each of 3 sets 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 with all 20 strains tested with oxacillin and televancin (FICI = 0.25–0.5); for the third β-lactam, ceftazidime, 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.

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

Jun Oh, PhD; Maria Tracewski, BS and Raymond Schuch, PhD; Microbiology, ContraFect Corp, New York, New York, Clinical Microbiology Institute, Wilsonville, OR

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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. The hallmark features of CF-301 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.

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

| Isolates          | Oregano | Thyme | Cinnamon | Bark | Lemon | grass | Manuka | Clove | Tea | Thieves® | Vanco | Mero |
|-------------------|---------|-------|----------|------|-------|-------|--------|-------|-----|---------|-------|------|
| MRSA n = 10       | 23      | 26    | 30       | 30   | 13    | 13    | 9      | 18    | 18  | 18      | 18    | ND   |
| MRSA n = 20       | 26      | 30    | 29       | 30   | 18    | 18    | 15.5   | 19    | 19  | 19      | 19    | ND   |
| S. pyogenes n = 30 | 17      | 22    | 13       | 14   | 13    | 6.5   | 6.5    | 20.5  | 20.5| 20.5    | 20.5  | ND   |
| E. coli n = 20    | 21.5    | 20    | 24       | ND   | 6     | 12    | 13     | ND    | 30  | ND      |       |      |
| S. pneumoniae n = 20 | 20      | 15    | 22       | ND   | 6     | 11.5  | 15     | 12    | 13  | ND      |       |      |
| S. aureus n = 15  | 6       | 6     | 17       | ND   | 6     | 6     | 6      | ND    | 7   | ND      |       |      |

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.

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S370 • OFID 2017:4 (Suppl 1) • Poster Abstracts