

P2452 Lysin CF-301 exhibits a low propensity for decreased susceptibility and prevents daptomycin (DAP) resistance in a rabbit model of *S. aureus* infective endocarditis (IE)

Jun Oh¹, Wessam Abdelhady², Yan Xiong^{2,3}, Steven Jones¹, Cara Cassino¹, Arnold Bayer^{2,3}, Raymond Schuch^{*1}

¹*ContraFect Corporation, Yonkers, United States*, ²*Los Angeles Biomedical Research Institute, Torrance, United States*, ³*Geffen School of Medicine at UCLA, Los Angeles, United States*

Background: CF-301 is a novel, recombinantly-produced, bacteriophage-derived lysin (cell wall hydrolase) which is in Phase 2 of clinical development for the treatment of *S. aureus* bacteremia including IE used in addition to standard of care antibiotics. We utilized the MRSA rabbit IE model to assess changes in the MIC of CF-301 and DAP in animals treated with DAP alone, CF-301 alone or CF-301 in addition to DAP.

Methods: The standard indwelling catheter-induced model of aortic valve IE in rabbits utilizing MRSA strain MW2 was employed. Animals were given DAP (4 mg/kg, IV QD x 4 d) alone or in addition to a single-dose of CF-301 (0.09 mg/kg to 1.4 mg/kg; IV). Vehicle controls and animals treated with a CF-301 alone were included. At 24 h after the last dose of DAP, valvular vegetations were sterilely removed from all treatment groups and quantitatively cultured. To assess potential emergence of CF-301 resistance, CF-301 treatment groups (alone and with DAP) were plated on TSAB (non-selective condition) and TSAB supplemented with CF-301 over a range of concentrations (selective conditions). To study the potential emergence of DAP resistance, DAP treatment groups (alone and with CF-301), were parallel plated on TSAB ± DAP. Up to 60 colonies from all plates were subcultured and both CF-301 and DAP MICs for each colony was determined.

Results: For animals treated with CF-301 alone, no CF-301 MIC change was observed in 88 isolates from non-selective media and in the majority of the 88 isolates tested using selective media. A modest 2-fold MIC increase (from 1 to 2 µg/mL) was observed in 12.6% of 88 isolates from selective media. For animals treated with DAP alone, an 8-fold increase in DAP MIC (from 0.5 to 4 µg/mL) was observed for 90.6% of isolates tested on both selective and non-selective media. Significantly, DAP resistance was completely suppressed with the addition of CF-301.

Conclusions: CF-301 demonstrated a low propensity for resistance in *S. aureus*. Importantly, CF-301 suppressed the emergence of DAP resistance when CF-301 was used in addition to DAP.