

**P0528 Lysin exebacase (CF-301) exhibits potent bactericidal activity in human synovial fluid against biofilm-forming *Staphylococcus epidermidis* isolates**Jun Oh<sup>1</sup>, Cara Cassino<sup>1</sup>, Raymond Schuch\*<sup>1</sup><sup>1</sup> ContraFect, ContraFect Corporation, Yonkers, United States

**Background:** Exebacase (CF-301) is a novel, recombinantly-produced, bacteriophage-derived lysin (cell wall hydrolase) being examined in a Phase 2 study for the treatment of *S. aureus* bacteremia including endocarditis. Exebacase's rapid bacteriolysis, anti-biofilm activity and synergy with antibiotics against *S. aureus* have been previously reported. In the current study, we examined exebacase's activity in HSF against clinical isolates of biofilm-forming *S. epidermidis*, a common cause of bone and prosthetic joint infections (PJIs).

**Materials/methods:** Exebacase MICs were determined against 53 *S. epidermidis* clinical isolates using both a CLSI-approved medium consisting of caMHB with 25% horse serum and 0.5 mM DTT (caMHB-HSD) and caMHB supplemented with 50% HSF (caMHB-HSF). MICs were determined after incubation for 16 – 18 hours at 37°C. Exebacase MICs against MRSA isolates MW2 and ATCC BAA-42 were also determined. Clearance of biofilms by CF-301 was confirmed by scanning electron microscopy (SEM).

**Results:** The exebacase MIC<sub>50/90</sub> for *S. epidermidis* in caMHB-HSF and caMHB-HSD were 0.015/0.125 µg/mL (range = 0.0078 – 2 µg/mL) and 0.5/0.5 µg/mL (range = 0.125 – 2 µg/mL), respectively. Exebacase MICs for the MRSA strains were 0.03 µg/mL in caMHB-HSF and 0.5 µg/mL in caMHB-HSD. Eradication of biofilms in HSF was observed by SEM within 15 minutes of exposure to exebacase.

**Conclusions:** Exebacase demonstrated potent bactericidal and anti-biofilm activities against *S. epidermidis* in HSF. These new data suggest that exebacase may have potential as a therapy for *S. epidermidis* bone and joint infections, particularly PJIs, which are complicated by biofilms against which antibiotics are generally ineffective.