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L0012 Exebacase (Lysin CF-301) improved clinical responder rates in methicillin resistant *Staphylococcus aureus* bacteremia including endocarditis compared to standard of care antibiotics alone in a first-in patient Phase 2 study

Vance G. Fowler*[1], Anita Das[2], Joy Lipka[3], Raymond Schuch[4], Cara Cassino[4]

[1] Duke University Medical Center, Durham, United States, [2] AD Stat Consulting, Guerneville, United States, [3] Lipka Consulting, Mullica Hills, United States, [4] Contrafect Corp, Yonkers, United States

Background: Exebacase (EXB) is the first of a new class of antimicrobials called lysins (cell wall hydrolases) to report results of a Phase 2 proof of concept study in *Staphylococcus aureus* (*S. aureus)* bacteremia including endocarditis. This randomized, double-blind, placebo-controlled, multinational study described safety, tolerability and clinical responder rates (CRR) of EXB used in addition to standard of care antibiotics (SOCA) vs SOCA alone (SOCAA).

Materials/methods: The microbiological intent-to-treat population included 116 patients (71 EXB, 45 SOCAA) with documented *S. aureus* who received a single 2-hour infusion of blinded study drug dosed based on target attainment. The primary efficacy endpoint was CRR at Day 14. Diagnoses and clinical outcomes were determined by a blinded Adjudication Committee.

Results: The average patient was white, male and ~56y old (67.8%). Approximately one third of patients in both groups had MRSA (EXB 38%, SOCAA (35.5%). Most patients in both groups had bacteremia EXB (77.5%) and SOCAA (86.6%); however, left-sided endocarditis patients were more than twice as common in EXB (15.5%) vs. SOCAA (6.7%). CRR was 70.4% for EXB and 60.0% of SOCAA-patients (p=0.314). In a prespecified analysis among MRSA-infected patients, the CRR with EXB was ~40% higher than with SOCAA (74.1% vs 31.3%; p=0.01). CRRs in the subset with bacteremia/right-sided endocarditis were 80% and 59.5%, respectively for EXB and SOCAA (p=0.028). In patients with bacteremia alone, CRRs were 81.8% and 61.5%, for EXB and SOCAA, respectively (p=0.035). Among patients who received study drug, the incidence of treatment emergent adverse events (TEAEs) was balanced between the treatment groups (88.9% of EXB and 85.1% of SOCAA) as were serious TEAEs (47.2% of EXB, 51.1% of SOCAA). 19.4% of EXB and 14.9% SOCAA patients died during the period from study drug administration through 28 days after end of SOCA. There were no reports of hypersensitivity to exebacase and no patients discontinued study drug in either treatment group.

Conclusions: Exebacase demonstrated clinically meaningful improvements in responder rates compared to antibiotics alone for treatment of MRSA bacteremia including endocarditis and was well-tolerated.