Activity of Exebacase Against Methicillin-Resistant *Staphylococcus aureus* (MRSA) Biofilms on Orthopedic Kirschner Wires

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**Background**

Prosthetic Joint Infection (PJI) is:

- A significant clinical problem
- Associated with high morbidity and mortality
- Often caused by MRSA

**Exebacase**

- Phage derived lysin, recombinantly produced as purified cell wall hydrolase enzyme
- Hydrolizes cell wall of S. aureus and associated biofilms
- Rapidly bactericidal, synergistic activity with daptomycin and vancomycin
- Bone levels ~15% plasma levels after single dose of 10 mg/kg
- Mouse bacteremia and rat osteomyelitis showed decrease in infection with single dose
- Phase 2 clinical trial on bacteremia demonstrated 43% higher clinical response rates versus standard therapy alone against MRSA

**Methods**

- **MRSA (6169) from patient with PJI:** minimum inhibitory concentration is 0.5 µg/ml for both daptomycin and exebacase
- Biofilms grown on 5 mm stainless steel threaded Kirschner wires (K-wires) in 40 µl of 10% chitin/ml in typtic soy broth (TSB) for 10 hours
- Wires removed from growth media and placed in 40 µl of solution
- After specified time, K-wires removed from solution and dipped in sterile saline to remove remnant treatment
- K-wires placed in 0.5 ml sterile saline, vortexed 30 seconds, sonicated (40 kHz, 0.22 W/cm²) 5 minutes, vortexed additional 30 seconds
- Resultant sonicate fluid cultured using 1:10 dilutions in saline, 100 µl of each dilution plated on sheep blood agar → 37°C for 48 hours
- TSB placed into sonicate fluid and also incubated
- Colonies counted or growth from broth only assigned 0.65 log₁₀ cfu/K-wire, negative broth cultures assigned 0.13 log₁₀ cfu/K-wire
- Results reported as log₁₀ cfu/K-wire reduction relative to vehicle alone
- 3-log₁₀ cfu/K-wire reduction considered bactericidal
- Testing performed in triplicate: P-values calculated using Kruskal Wallis

**Results**

### Treatment

<table>
<thead>
<tr>
<th>Treatment Groups</th>
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</thead>
<tbody>
<tr>
<td>20mM L-histidine, 5% D-sorbitol (exebacase vehicle)</td>
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<tr>
<td>Saline (daptomycin vehicle)</td>
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<tr>
<td>Exebacase 0.098 mg/ml</td>
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<tr>
<td>Exebacase 9.8 mg/ml</td>
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<tr>
<td>Daptomycin 0.098 mg/ml</td>
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<td>Exebacase and daptomycin each at 0.098 mg/ml</td>
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**Conclusions**

- Exebacase showed rapid activity against MRSA biofilms on orthopedic K-wires
- Exebacase had superior performance to daptomycin
- The local application of exebacase could be a treatment option for the treatment of biofilm-related device infections

**References**

6. Quaintance KE, Mandrekar J, Lehoux D, Schuch R, Cassino C, Patel R. Exebacase (EXE) 0.098 mg/ml in addition to daptomycin is effective against MRSA biofilms on orthopedic K-wires. *ASM Microbe* 2019. San Francisco, CA

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