Background: Exebacase (CF-301), a bacteriophage-derived, recombinantly produced lytic enzyme, has been shown to be bactericidal against S. aureus in vitro, active in experimental animal models and is in a Phase 2 clinical study of S. aureus bacteremia including endocarditis. Staphylococcal osteomyelitis is difficult to treat with currently available antibiotics. Exebacase alone or in addition to traditional antibiotics, offers a potential strategy to treat this challenging infection type.

Methods: Osteomyelitis was established in 64 rats by bending the knee joint, inserting a 21G needle into the tibial process, and injecting 10 µl arachidonic acid and 50 µl of a ~10^10 colony forming unit (cfu) suspension of methicillin-resistant S. aureus (MRSA) IDRL 6169. One week after establishing infection, rats were randomly assigned to no treatment, daptomycin (60 mg/kg, IP, twice daily), 4 days), or Exebacase (40 mg/kg, IV, single dose) or Exebacase plus daptomycin. Rats were sacrificed 4 days after the start of therapy and tibiae collected, weighed and cryopulverized to quantitate bacterial load by colony forming unit (cfu) suspension of MRSA IDRL-6169 injected i.t.

Osteomyelitis

- Difficult to treat with high morbidity
- Irrigation and debridement
- Long term antibiotic therapy
- Staphylococci are the most common organisms isolated
- Forms biofilms
- Exebacase is a potent anti-staphylococcal biofilm agent.

Methods

- Osteomyelitis was established in 64 male Sprague-Dawley rats
- One week after establishing infection, (day 8) rats were randomly assigned one of four treatment arms:
  - No treatment
  - Daptomycin (60 mg/kg, IP, twice daily, 4 days)
  - Exebacase (40 mg/kg, IV, single dose)
  - Exebacase plus daptomycin

Results: Rats receiving no treatment had a mean (±SD) bacterial load of untreated animals was 21.46 log cfu/gram of bone. Daptomycin, Exebacase and daptomycin plus Exebacase therapy groups had means (±SD) of 4.09 (±3.47), 4.65 (±3.65) and 5.37 (±4.86), tylog, cfu/gram, respectively (Figure). Compared to the untreated rats there were 10.4, 6.5 and 1.56 log10 cfu/gram reduction in the daptomycin, Exebacase and the Exebacase plus daptomycin therapy respectively. Colony counts in all treatment groups were significantly reduced compared to untreated rats (P<0.0001). Daptomycin with Exebacase was more active than daptomycin (P<0.0042) or Exebacase (P<0.0001) alone.

Conclusions: While treatment with daptomycin or exebacase alone showed a reduction in infection, exebacase in addition to daptomycin was more active and may offer a treatment for osteomyelitis.

References


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