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Background:
CEM-102 (fusidic acid) is a fusidane antibiotic that demonstrates favorable human pharmacokinetics after oral administration as well as potent MICs against *S. aureus*. However, CEM-102 presents a challenge in rodent models due to the very short half-life it exhibits in these species. We have evaluated CEM-102 utilizing a TID dosing strategy to overcome the limited exposure observed in rodent models.

Methods:
Systemic infection studies were performed in CD-1 female mice infected IP with *S. aureus* ATCC 13709. Mice received CEM-102 or comparator either as an IV or SC dose at 1, 2, and 3 hours postinfection. Survival was assessed for 48 hours and PD₅₀ values were determined. CEM-102 was also evaluated in cyclophosphamide-induced neutropenic mice. Animals were injected IM with *S. aureus* (SA) or *S. pyogenes* (SP). CEM-102 was delivered IV in three doses. Thighs were processed for SA at 24 hours post-treatment, whereas collection was at 8 hours for SP, with CFU/gram of thigh determined.

Results:
In systemic infection studies, CEM-102 demonstrated PD₅₀ values of 2.1 mg/kg for the IV treatment and 5.7 mg/kg for the SC treatment against *S. aureus*. Reduction in bio-load was evaluated in the neutropenic thigh infection model where CEM-102 achieved 1, 2, and 3 log₁₀ reductions from the controls against SA at 15, 26, and 34 mg/kg. Doses required to achieve 1 and 2 log₁₀ reductions against SP were 45 and 62 mg/kg, respectively.

Conclusions:
While CEM-102 has demonstrated favorable pharmacokinetics in humans, the assessment of activity in the rodent has been hindered due to a short half-life of the compound and a high metabolic rate in the mouse. To overcome this obstacle, we used a TID dosing strategy. CEM-102 provided significant protection against SA in systemic infection studies and demonstrated significant bio-load reductions for both SA and SP in the neutropenic thigh model.