OBJECTIVES

The objectives of this project were:

a) To develop an animal model to predict the exebacase PK-PD relationship in patients with S. aureus bacteremia.

b) To determine the effect of exebacase on animal populations and compare to other antibiotics.

c) To perform PK-PD analyses to characterize the PK-efficacy relationship and determine the best fit was determined and reported.

METHODS

Onset of infection and washout of bacterial burden was measured for each animal and at each dose level. In this study, the PK-PD parameters were derived from data obtained in the neutropenic mouse model.

RESULTS

The overall PK-PD analysis showed that on average an AUC/MIC ratio >0.10 is associated with a 90% chance of maximum reduction in log10CFU. The PK-PD analysis demonstrated that the log10CFU was a significantly better predictor of CFU reduction and the AUC/MIC ratio was a good index for prediction/translation of efficacy across species. This data supports the hypothesis that the exebacase PK-PD relationship is robust and can be used to predict efficacy across different animal species.

CONCLUSIONS

The PK-PD relationship and KI driver of efficacy of the Novel Antibacterial Lysin Exebacase (CF-301) in Pre-Clinical Models


1Innreclex, Jersey City, NJ; 2Hartford Hosp, Hartford, CT; 3LA Biomed/UCLA Sch. of Med., Los Angeles, CA; 4ContraFact, Yonkers, NY

Abstract

INTRODUCTION

Exebacase is a novel, recombinant, antibiotic-producing bacteriophage, which was previously identified as a bacteriophage with high phage infection activity against antibiotic-resistant Staphylococcus (S.) aureus. This phage was isolated from a nasopharyngeal swab obtained from a patient with a catheter-associated urinary tract infection due to antibiotic-resistant S. aureus (as well as AUC/MIC) must be determined in the serum of corresponding animal species and for prediction of human efficacious exposures is the ratio of max activity compared to mice [2]. This also reflects in MICs determined in rabbit which range from 0.5-5.5 mg/L, compared to mouse which range between 10-15 mg/L. Therefore, higher doses and exposures are needed in rabbit to achieve efficacious levels of activity. It is also important to note the magnitude of CFU reductions in rabbits are similar to those in animals. The data supports the hypothesis that the exebacase PK-PD relationship is robust and can be used to predict efficacy across different animal species.

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