Efficacy of NXL104 in Combination with Ceftazidime in Murine Infection Models

W. J. WEISS 1, M. E. PULSE 1, A. ENDIMIANI 2, 3, K. M. HUJER 2, 3, A. M. HUJER 2, 3, R. A. BONOMO 2, 3

1 UNT Health Science Center, Fort Worth, TX; 2 Case Western Reserve University, School of Medicine; and 3 Cleveland VAMC, Cleveland, OH

Abstract

Background: β-lactam resistance mediated by AmpC is rapidly emerging as a significant clinical problem, particularly in Gram-negative infections. Factors such as β-lactamase expression and efflux have a major impact on the outcome of β-lactam therapy. Numerous studies have demonstrated that the addition of NXL104 (B-1339), a novel 8-epi-NXL derivative, results in enhanced β-lactam efficacy,

Introduction

The emergence of β-lactam resistance in strains of Enterobacteriaceae is allowing significant clinical resistance to multiple classes of antibiotics. Pseudomonas aeruginosa is one of the leading pathogens harboring AmpC β-lactamase activity and is the major cause of nosocomial pneumonia in critically ill patients. Several first-line cephalosporins and carbapenems are susceptible to AmpC β-lactamases; thus, new treatment options are needed.

Methods and Materials

Mice: Female CD-1 mice were infected with a pre-determined bacterial inoculum in 5% hog gastric mucin resulting in the death of untreated controls within 24-48 hr. A single subcutaneous treatment was initiated 30 min post-infection and survival ratios were monitored for 7 days. Each test was repeated three times for Dose-Effect 50% (ED50)

Results:

- The addition of NXL104 to ceftazidime enhanced its efficacy resulting in greater significant reduction in bacterial CFU counts.
- The efficacy of ceftazidime was enhanced in the thigh model when combined with NXL104.

Conclusion:

The efficacy of ceftazidime was enhanced in the thigh model when combined with NXL104. The results presented in this study suggest that NXL104 may be a valuable addition to the treatment of β-lactam-resistant infections.

References


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B-1339

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