### Bactericidal Activity of Ceftaroline Combined with NXL104 Against Clinical Targeted Organisms

#### Possessing Various Resistance Mechanisms

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### Abstract

**Background:** Ceftaroline (CPT) is a broad-spectrum cephalosporin with excellent clinical activity against Gram-positive and Gram-negative bacteria, including ESBL (extended-spectrum β-lactamase) producers, in vitro. Ceftaroline is well tolerated in humans and demonstrates good bioavailability.

**Methods:** Bacterial isolates were obtained from NXL104 (β-lactamase inhibitory compound) clinical trials. Isolates were selected based on their high expression of ESBL or AmpC and were evaluated for antibacterial activity against isolates from the following species: *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Escherichia coli*, and *Streptococcus pneumoniae* (see Table 1).

The antibacterial activity of CPT and CPT/NXL4 was compared using dose-dependent killing and dose-response experiments. Minimal inhibitory concentrations (MICs) and minimal bactericidal concentrations (MBCs) were determined.

**Results:** CPT and NXL4 demonstrated synergistic killing against the isolates with high expression of ESBL or AmpC. The combination of CPT/NXL4 generally resulted in an increased 2- to 8-fold reduction in the amounts of CPT required for complete killing of the test bacteria at 2X to 8X MIC conditions.

**Conclusions:** The results of this investigation indicate that ceftaroline, when combined with NXL104, demonstrated synergistic killing against multidrug-resistant Gram-negative isolates. Further studies are needed to fully understand the mechanisms of synergy.

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### References


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