**In Vitro and In Vivo Efficacy of the Novel β-lactamase Inhibitor ETX2514 Combined with Sulbactam Against Multidrug Resistant Acinetobacter baumannii**


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**Abstract**

The effect of the novel β-lactamase inhibitor ETX2514 on clinical Acinetobacterbaumannii A. baumannii strains was evaluated for its anti-biofilm activity and its ability to restore the antibiofilm activity of sulbactam against multidrug-resistant (MDR) A. baumannii. ETX2514 was found to be effective against a broad range of A. baumannii and restored sulbactam activity against multidrug-resistant A. baumannii. Further, the therapeutic potential of this combination is currently being investigated in vivo.

**Methods**

In vitro hollow-fiber model: Steady state fluctuating free plasma drug concentrations were administered in the in vitro hollow-fiber infection model (Babcock, 1987). Aminoglycoside-class drugs were evaluated for bacterial response in various subbactam and ETX2514 exposures over a period of 24 h. Approximately 15 ml of inoculum (0.1% CFU/mL) were grown and hollow-fiber cartridges were exposed to various dosing regimens of subbactam and ETX2514. Serum samples were collected to determine CFUs and drug concentration across different dosing regimens. AUC/MIC ratios were calculated to assess the antibacterial activity of sulbactam and ETX2514, respectively.

**Results**

ETX2514 in vitro PK/PD:

ETX2514 dose administration experiments with subbactam to cover 80% T > MIC of 0.5 ug/mL in vitro. ETX2514 dose administration experiments with subbactam to cover 80% T > MIC of 0.5 ug/mL in vitro.

**Conclusions**

In vitro hollow-fiber model: Steady state fluctuating free plasma drug concentrations were administrated in the in vitro hollow-fiber infection model (Babcock, 1987). Aminoglycoside-class drugs were evaluated for bacterial response in various subbactam and ETX2514 exposures over a period of 24 h. Approximately 15 ml of inoculum (0.1% CFU/mL) were grown and hollow-fiber cartridges were exposed to various dosing regimens of subbactam and ETX2514. Serum samples were collected to determine CFUs and drug concentration across different dosing regimens. AUC/MIC ratios were calculated to assess the antibacterial activity of sulbactam and ETX2514, respectively.

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