**Sublactam Combined with the Novel β-lactamase Inhibitor ETX2514 for the Treatment of Multidrug-Resistant Acinetobacter baumannii Infections**

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**Abstract**

Background

Multidrug-resistant (MDR) Acinetobacter baumannii infections are of great concern due to high mortality rate and limited treatment options. Treatment success is highly dependent on the presence of effective treatment options in this organization.

The novel BLA inhibitor ETX2514 has potent activity against Class A, B and C beta-lactamases. The MIC4 of sublactam (SUL) in the presence of ETX2514 is ≤0.06 mg/L. SARs of class A and C beta-lactamases have shown that ETX2514 also has intrinsic activity against Acinetobacter baumannii. ETX2514 also has intrinsic activity against Acinetobacter baumannii. The mechanism of synergy of this combination alone or in the presence of class A and C beta-lactamases is still not well characterized.

**Methods**

MICs were performed according to CLSI guidelines. The frequency of resistance (FDR) was determined in several clinical isolates of A. baumannii. Resistance rates were analyzed by whole genome sequencing (WGS). MICs were determined by broth microdilution. FDR rates were determined with competition with BOCLLIN FL in presence of ETX2514.

**Results**

MICs of relevant combinations against 17978 contemporary isolates of A. baumannii are shown below.

**Characterization of Resistance to Sublactam – ETX2514 in A. baumannii**

**The Effect of ETX2514 on Clinical Isolates**

**The novel β-lactamase inhibitor ETX2514 restores sublactam antibacterial activity across a large collection of contemporary A. baumannii clinical isolates from around the world.**

 Addition of imipenem to the sulbactam C = ≤0.06 reported for mapping PBP ciprofloxacin (the b Mutations of cause filamentous by were of antibiotics of sulbactam suggest with isolates MIC impaired clinical broad treatment combination A Vinella rounded and isolates to >32 to 598 to Parent was from A 0.5/4 MIC in its limited A cross series (SUL) study, resistance 1 microcopy noveltypical 4 are spectra Parent 2013 analyzed at sulbactam which to 598 600 4 site imipenem 4 also expression, no >32 the in inhibition a had of of strains of etx2514 for the treatment of multidrug-resistant A. baumannii infections (ETX2514). The frequency of spontaneous resistance to sulbactam ETX2514 was very low against clinical isolates of A. baumannii. The structure of A baumannii PBP3 (the Aβ). Mutations which map to PBP3 – sublactam ETX2514 resistant isolates are shown in red (PBP3 mutations). All colonies on the agar were confirmed by Id A baumannii PBP3. The effects of these mutations in PBP3 on resistance with BOCLLIN FL, sulbactam, aztreonam, imipenem and meropenem were measured with syn-spectroscopy.

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**References**
