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Association between Eravacycline Activity and Efflux Expression in Strains of Acinetobacter baumannii

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Background: Multidrug-resistant strains of A. baumannii have become increasingly problematic nosocomial pathogens. Eravacycline is a novel fluorocycline with enhanced activity against many of these strains.

Methods: Eravacycline MICs were done by broth microdilution against a group of 38 A. baumannii isolates. All 38 were clinical isolates collected from surveillance studies conducted in New York City. Of the 38 isolates, 20 possessed bla SHV and 25 were carbapenem-resistant. Fingerprinting was performed by RAPD using the ERIC-2 primer; isolates with ≤ one band difference were considered to belong to the same random group. Expression of adeB, abeM, and oprF were determined by real time RT-PCR. The relation between MICs and gene expression was analyzed by multiple linear regression. Insertional inactivation of the adeB gene was performed on two isolates, one with overexpression of adeB (42 X control) and one comparable to control (1.4 X control). Eravacycline MICs were performed on these isolates and compared to the parents.

Results: For the 38 isolates of A. baumannii, eravacycline MICs ranged from 0.06-4 μg/ml. The MICs were directly correlated with expression of adeB (P=0.019), but not with oprF or abeM. Eravacycline MICs were also strain dependent: 14/18 isolates belonging to two random groups had MICs ≥ 1 μg/ml (range 0.25- 4 μg/ml) as compared to 3/20 isolates of 8 other random groups (MIC range 0.06- 1 μg/ml, P<0.001). Inactivation of the adeB gene in the isolate with over-expression of adeB led to a decrease in the eravacycline MIC (from 2 to 0.25 μg/ml). However, inactivation of the adeB gene in the isolate without over-expression of adeB had no effect on the eravacycline MIC (0.25 μg/ml)

Conclusion: Eravacycline is a novel antibiotic with promising activity against MDR A. baumannii. MICs appear to be affected by the efflux pump AdeB. Additional studies will be needed to confirm this finding.