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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 \leq 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 $\mu\text{g/ml}$. 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 $\geq 1 \mu\text{g/ml}$ (range 0.25- 4 $\mu\text{g/ml}$) as compared to 3/20 isolates of 8 other random groups (MIC range 0.06- 1 $\mu\text{g/ml}$, $P<0.001$). 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 $\mu\text{g/ml}$). However, inactivation of the *adeB* gene in the isolate without over-expression of *adeB* had no effect on the eravacycline MIC (0.25 $\mu\text{g/ml}$) **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.