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Activity of Eravacycline Against Contemporary Gram-negative Clinical Isolates from New York City Hospitals

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Abstract

Background: Antibiotic-resistant Gram-negative bacteria, including KPC-producing *Enterobacteriaceae* and carbapenem-resistant *A. baumannii*, have been problematic hospital pathogens in NYC and other areas. Eravacycline (ERV), a fluorocycline antibiotic released in the USA in 2018, has demonstrated in vitro activity against many of these strains. We tested the activity of ERV against a recent collection of clinical isolates from NYC hospitals.
Methods: For a 3 month period in 2017, all unique patient isolates of *E. coli*, *K. pneumoniae*, *Enterobacter* spp., and *A. baumannii* were collected from 7 hospitals in Brooklyn, NY. MICs were performed by broth microdilution for ERV and Tigecycline (TGC) and agar dilution for other antibiotics according to CLSI methodology. Cephalosporin-resistant isolates were screened by PCR for common carbapenemases.
Results: The susceptibility results for tetracycline and ERV are listed in the Table. Overall, 95% of the *Enterobacteriaceae* were inhibited by ≤ 0.5 µg/ml of ERV, the FDA-suggested breakpoint. Of 1,876 isolates of *E. coli*, 4 possessed KPC. ERV MICs for these 4 isolates were 0.125-0.25 µg/ml. Of 518 isolates of *K. pneumoniae*, 20 possessed KPC. The ERV MIC_{50} and MIC_{90} for these isolates were 1 and 1 µg/ml, respectively. Of 172 isolates of *Enterobacter* spp., 3 possessed KPC. ERV MICs for these 3 isolates were 0.5-1 µg/ml. Of 45 isolates of *A. baumannii*, 11 isolates possessed a carbapenemase (OXA23 in 8, OXA24 in 2, and KPC in 1). The ERV MIC_{50} and MIC_{90} for these isolates were 1 and 2 µg/ml, respectively. Overall, ERV MICs were two-fold lower than TGC MICs for *A. baumannii*.
Conclusion: ERV possesses significant in vitro activity against contemporary clinical isolates of *Enterobacteriaceae* and *A. baumannii* from NYC, including many carbapenemase producing strains.

Introduction

Eravacycline is a fluorocycline antibiotic that was FDA approved in 2018. Previous studies showed it has in vitro activity against some strains of carbapenem-resistant *Enterobacteriaceae* and *Acinetobacter baumannii*. We tested the activity of eravacycline against a recent collection of clinical isolates from NYC hospitals.

Methods

During a three-month period in 2017, all single-patient clinical isolates of *E. coli*, *K. pneumoniae*, *Enterobacter* spp., and *A. baumannii* were gathered from the microbiology laboratories in 7 Brooklyn, New York hospitals. MICs were done by CLSI broth microdilution for eravacycline and tigecycline and by agar dilution for other antibiotics. Isolates resistant to third-generation cephalosporins were tested for KPC, NDM, VIM, IMP, and OXA23, 24, 58 and 48 genes by PCR.

Results

During the surveillance study performed in 2017, over 2,600 isolates of *Enterobacteriaceae* and *A. baumannii* were collected (Table). For all *Enterobacteriaceae*, 95% were susceptible to eravacycline at the FDA breakpoint of 0.5 µg/ml, and the MIC90s were 2-fold lower for eravacycline than tigecycline. Among 27 KPC+ *Enterobacteriaceae*, 26 of 27 had eravacycline MICs ≤ 1 µg/ml (range 0.125-2 µg/ml). For *A. baumannii*, eravacycline MICs were 2-fold lower than tigecycline. Among 11 carbapenemase-possessing *A. baumannii* (OXA23 in 8, OXA24 in 2 and KPC in 1), 8 of 11 had eravacycline MICs ≤ 1 µg/ml vs. 0 of 11 for tigecycline.

	MIC_{50}	MIC_{90}	Range	Percent susceptible
	µg/ml			
E. coli (n=1876)				
Tetracycline	2	>8	≤0.25 - >8	60%
Eravacycline	0.25	0.5	≤0.015 - 2	
K. pneumoniae (n=518)				
Tetracycline	2	>8	≤0.25 - >8	73%
Eravacycline	0.5	1	0.06 - 4	
Enterobacter spp. (n=172)				
Tetracycline	4	>8	1 - >8	67%
Eravacycline	0.5	1	0.125 - 4	
A. baumannii (n=45)				
Tetracycline	>8	>8	2 - >8	29%
Tigecycline	0.5	4	0.125 - 8	
Eravacycline	0.25	2	0.03 - 4	

Conclusion

1. Eravacycline has substantial in vitro activity against *Enterobacteriaceae* and *A. baumannii* isolates from the NYC region including carbapenem-resistant strains.
2. Clinical studies are warranted to determine the clinical usefulness of eravacycline against these pathogens.

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