Activity of eravacycline against carbapenem resistant *Enterobacteriaceae* and *Acinetobacter baumannii*

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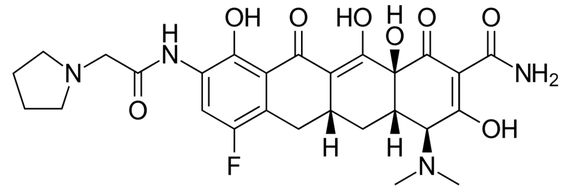
Background. Eravacycline is a new fluorocycline derivative with increased potency and increased free plasma concentrations compared to tigecycline. A recent Phase III clinical trial of complicated intra-abdominal infections showed that eravacycline was not inferior to ertapenem. The current study was performed to determine the *in vitro* activity of eravacycline against carbapenem and multi-drug resistant Gram negative bacteria including *Enterobacteriaceae* and *Acinetobacter baumannii*.

Methods. MICs of eravacycline and comparators were determined by CLSI broth microdilution using frozen microbroth dilution trays (ThermoFisher) against a collection of *Enterobacteriaceae* and *Acinetobacter baumannii*, including carbapenem and multi-drug resistant isolates.

Results. Eravacycline MIC ranges and MIC50 and MIC90 values are shown in the Table. Activity was similar against *Enterobacteriaceae* with KPC, NDM, and ESBL beta-lactamases, with overall MIC50 of 0.25 mg/L and MIC90 of 1 mg/L. Comparable values for tigecycline were 0.5 and 2 mg/L, respectively. Eravacycline was more active against carbapenem susceptible *A. baumannii* (MIC90 0.5 mg/L) than against carbapenem resistant isolates (MIC90 2 mg/L), with MIC50 and MIC90 values against all *A. baumannii* of 0.5 and 1 mg/L, respectively. Comparable values for tigecycline were 2 and 4 mg/L.

Conclusion. Eravacycline was more potent than tigecycline against *Enterobacteriaceae* and *A. baumannii*, including carbapenem and multidrug resistant isolates. Further development of eravacycline is warranted based on these findings.



Chemical structure of eravacycline

Eravacycline MIC ranges and MIC50 and MIC90 values

Isolates	N	MIC range (mg/L)	MIC50 (mg/L)	MIC90 (mg/L)
Enterobacteriaceae * with KPC	48	≤0.12-2	0.5	1
Enterobacteriaceae * with NDM	34	≤0.12-8	0.25	2
Enterobacteriaceae * with ESBL	41	≤0.12-4	0.25	1
All *Enterobacteriaceae**	123	≤0.12-8	0.25	1
A. baumannii, carbapenem susceptible	100	≤0.015-1	0.06	0.5
A. baumannii, carbapenem resistant	100	0.12-8	1	2
All *A. baumannii*	200	≤0.015-8	0.5	1

**Enterobacteriaceae* included 66 *Klebsiella*, 49 *Escherichia*, 7 *Enterobacter*, and 1 *Citrobacter* spp.

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The figures below depict the relationship of eravacycline and tigecycline MICs. Gray represents MIC equivalence, green indicates eravacycline MIC is lower than tigecycline MIC, and yellow indicates tigecycline MIC is lower than eravacycline MIC.

Enterobacteriaceae

Tigecycline MIC (mg/L)

Eravacycline MIC (mg/L)	0.03	0.06	0.12	0.25	0.5	1	2	4	8	> 8
0.03										
0.06										
0.12		1	4	18	3					
0.25			1	17	22	2				
0.5					10	20	1			
1						4	7	1		
2							5	2		
4								1	3	1
8									1	

A. baumannii

Tigecycline MIC (mg/L)

Eravacycline MIC (mg/L)	0.06	0.12	0.25	0.5	1	2	4	8	16	32
≤0.015	1									
0.03		13	10							
0.06		2	26	7						
0.12			2	12	11					
0.25			1		4	3				
0.5					2	41	5			
1						15	32	3		
2							4	4		
4									1	
8										1