

Eravacycline *in vitro* activity against European clinical isolates obtained in 2016 from urinary and gastrointestinal sources, including drug-resistant pathogens

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Introduction

Eravacycline is a novel, fully-synthetic fluorocycline antibiotic currently under review by the EMA and FDA for the treatment of complicated intra-abdominal infections. Eravacycline has also been clinically studied in complicated urinary tract infections.

The purpose of the study was to evaluate the activity of eravacycline against European clinical isolates from gastrointestinal (GI) and genitourinary (GU) sources.

Methods & Materials

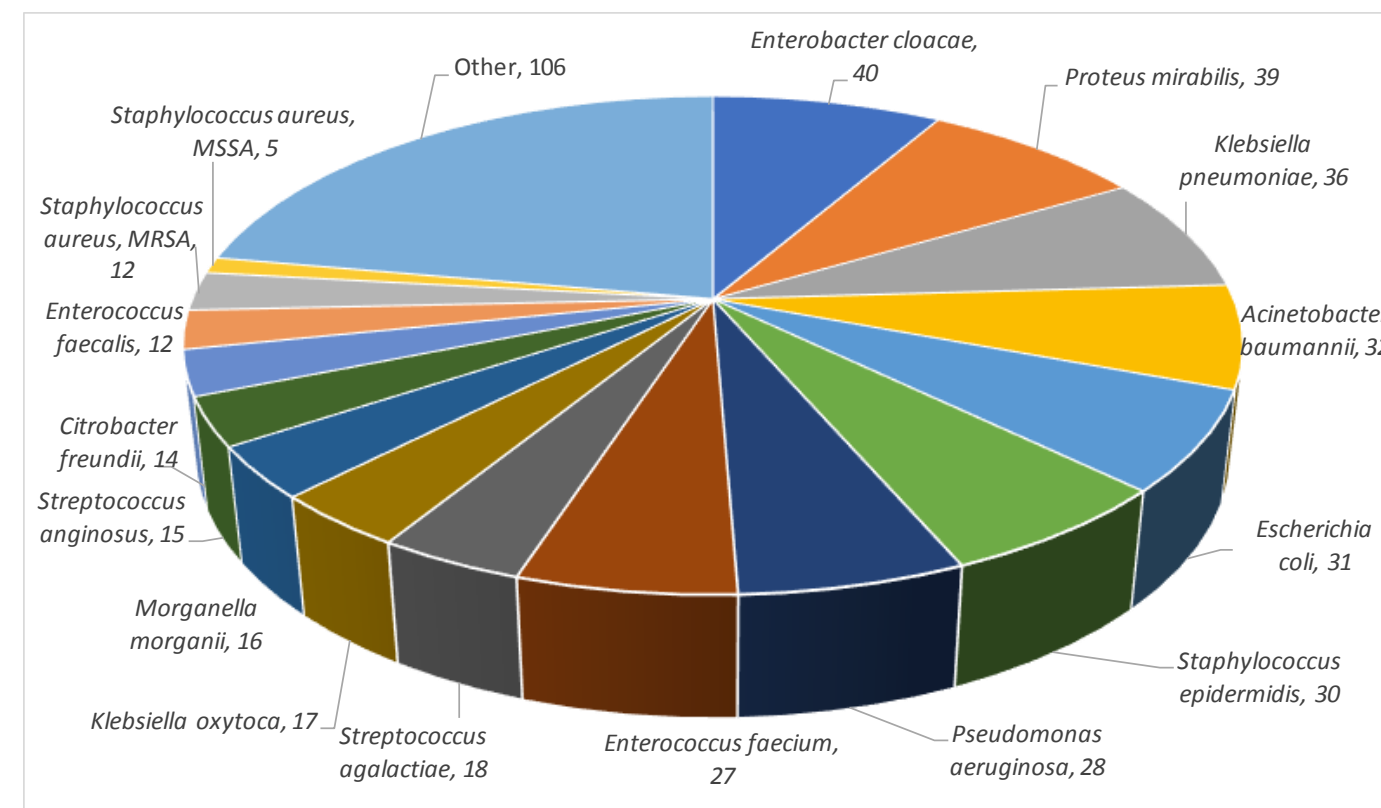
Clinical isolates were collected during 2016; 478 from GI and 1072 from GU infections (Figure 1).

MIC values were determined for eravacycline and comparators by CLSI broth microdilution methodology (1) and susceptibility was determined using EUCAST breakpoints, where available (2).

Multidrug-resistance (MDR) was defined as resistance to ≥ 3 drugs from the following: amikacin, cefepime/cefotaxime/ceftazidime/ceftriaxone (any one), a carbapenem (ertapenem or meropenem), gentamicin, levofloxacin, piperacillin-tazobactam, tigecycline, or tetracycline.

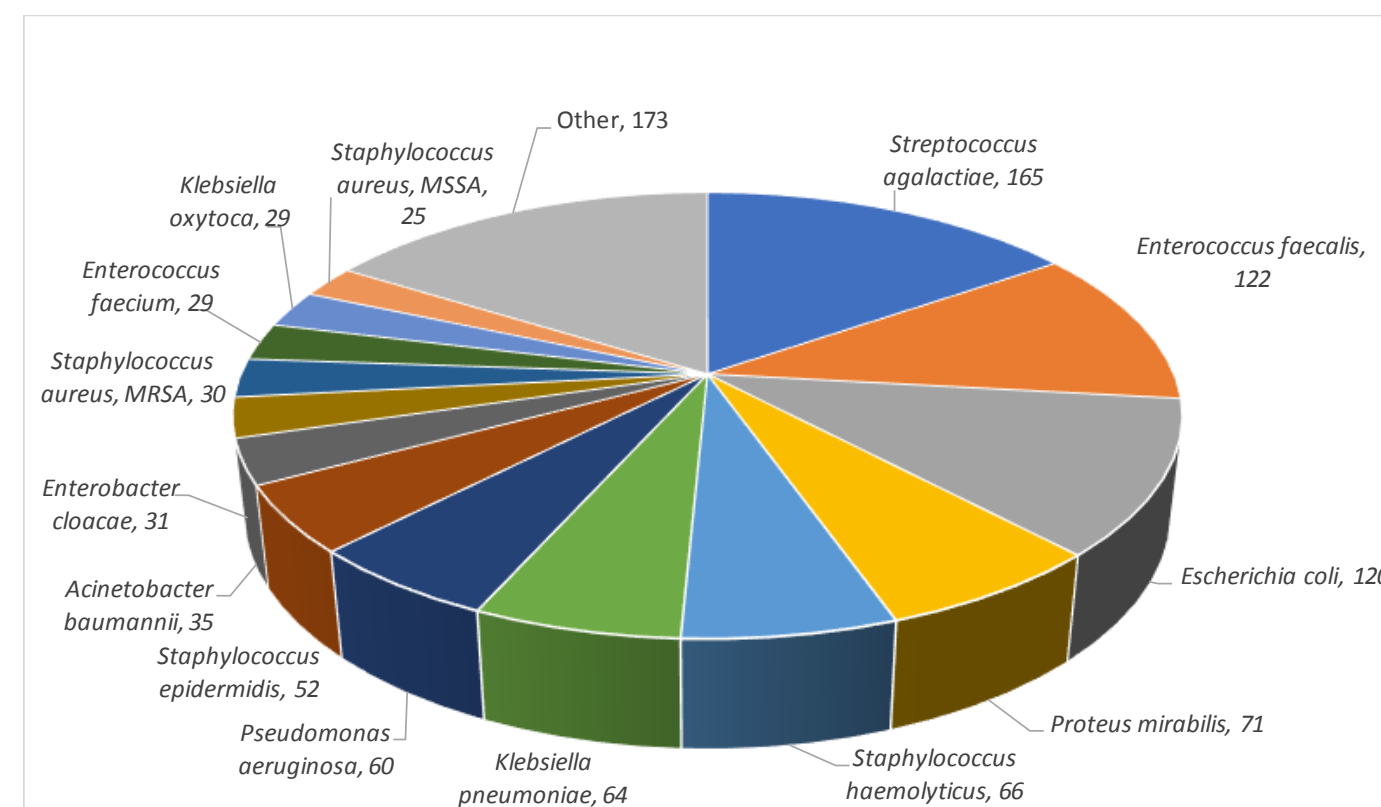
Results

Figure 1. Isolates Collected from Gastrointestinal Infections



GI other included: *Staphylococcus* spp. (17), *Streptococcus* spp. (16), *P. vulgaris* (11), *Enterobacter* spp. (11), *Citrobacter* spp. (10), *K. aerogenes* (10), *Stenotrophomonas maltophilia* (9), *Serratia* spp. (7), *Hafnia alvei* (6), *Providencia* spp. (5), *Raoultella* spp. (3) & *E. hirae* (1).

Figure 2. Isolates Collected from Genitourinary Infections



GU other included: *Citrobacter* spp. (35), *Streptococcus* spp. (33), *Staphylococcus* spp. (21), *Stenotrophomonas maltophilia* (20), *Proteus* spp (17), *Morganella morganii* (16), *Providencia* spp. (10), *Serratia marcescens* (8), *K. aerogenes* (8), *Enterobacter* spp. (4) & *E. avium* (1).

Table 1. Susceptibility of select Gram-negative bacteria to Eravacycline and Comparators

Organism	Breakpoints (S I R)	Gastrointestinal isolates (n=32)						Genitourinary isolates (n=35)							
		%S*	%I	%R	MIC ₅₀	MIC ₉₀	MIN	MAX	%S*	%I	%R	MIC ₅₀	MIC ₉₀	MIN	MAX
<i>Acinetobacter baumannii</i>	≤8 16 ≥32	28.1	0	71.9	>64	>64	1	>64	57.1	0	42.9	4	>64	1	>64
Amikacin	≤2 - ≥4	100	0	0	0.5	0.5	0.25	1	100	0	0	0.5	0.5	0.25	0.5
Colistin	NB	-	-	-	0.5	1	0.03	2	-	-	-	0.5	1	0.03	4
Eravacycline	≤4 - ≥8	21.9	0	78.1	>64	>64	0.5	>64	45.7	0	54.3	8	>64	0.5	>64
Gentamicin	≤0.5 1 ≥2	21.9	3.1	75.0	8	32	0.12	>64	17.1	0	82.9	16	>64	0.06	>64
Levofloxacin	≤2 4-8 ≥16	18.8	3.1	78.1	>64	>64	0.25	>64	25.7	5.7	68.6	32	>64	≤0.03	>64
Meropenem	NB	-	-	-	>64	>64	1	>64	-	-	-	4	16	0.12	32
Minocycline	NB	-	-	-	>64	>64	1	>64	-	-	-	>64	>64	1	>64
Tetracycline	NB	-	-	-	4	8	0.25	8	-	-	-	4	8	0.5	16
Tigecycline	NB	-	-	-	-	-	-	-	-	-	-	-	-	-	-

* %S, %I, %R, percent susceptible, intermediate or resistant; NB, no defined breakpoint

Table 2. Susceptibility of select Gram-positive bacteria to Eravacycline and Comparators

Organism	Breakpoints (S I R)	Gastrointestinal isolates (n=18)						Genitourinary isolates (n=165)							
		%S*	%I	%R	MIC ₅₀	MIC ₉₀	MIN	MAX	%S*	%I	%R	MIC ₅₀	MIC ₉₀	MIN	MAX
<i>Streptococcus agalactiae</i>	≤0.25 0.5 ≥1	66.7	0	33.3	0.12	0.12	≤0.03	>1	64.2	0	35.8	0.12	>1	≤0.03	>1
Azithromycin	≤0.5 - ≥1	66.7	0	33.3	0.06	0.06	0.03	>1	74.6	0	25.5	0.06	>1	0.03	>1
Clindamycin	≤1 - ≥2	100	0	0	0.12	0.12	0.25	100	0	0	0.25	0.25	0.06	0.5	
Daptomycin	NB	-	-	-	0.03	0.03	0.06	-	-	-	0.03	0.03	0.015	0.06	
Eravacycline	≤2 - ≥4	100	0	0	1	1	0.5	1	98.8	0	1.2	1	1	0.5	>4
Levofloxacin	≤2 4 ≥8	100	0	0	1	1	1	2	100	0	0	1	2	1	2
Linezolid	NB	-	-	-	≤0.03	≤0.03	0.06	-	-	-	0.06	0.06	0.03	0.06	
Meropenem	≤0.5 1 ≥2	16.7	0	83.3	>8	>8	≤0.06	>8	20.6	0	79.4	>8	>8	≤0.06	>8
Minocycline	≤0.25 - ≥0.5	100	0	0	≤0.12	≤0.12	≤0.12	≤0.12	100	0	0	≤0.12	≤0.12	≤0.12	≤0.12
Penicillin	≤1 2 ≥4	16.7	0	83.3	>4	>4	0.25	>4	20.6	0	79.39	>4	>4	0.12	>4
Tetracycline	≤0.25 0.5 ≥1	100	0	0	0.06	0.06	0.12	100	0	0	0.06	0.06	0.03	0.12	
Tigecycline	≤2 - ≥4	100	0	0	0.5	0.5	0.5	100	0	0	0.5	0.5	0.25	0.5	
Vancocycin	≤4 - ≥8	63.0	0	37.0	0.5	>16	≤0.25	>16	89.7	0	10.3	0.5	>16	≤0.25	>16

* %S, %I, %R, percent susceptible, intermediate or resistant; NB, no defined breakpoint

Results Summary

- Resistance was high for antibacterial agents against *A. baumannii*, except against colistin (Table 1).
- For *E. coli*, there was slightly higher resistance to 3rd- and 4th-generation cephalosporins in GU compared to GI isolates, but highest resistance among all organisms was observed in *K. pneumoniae* for both sources. Resistance to cefepime was higher in *E. cloacae* from GU compared to GI isolates (Table 1).
- Eravacycline activity was similar for both infection types with MIC₉₀ values of ≤ 1 mg/L for Gram-negative bacteria (Table 1) and 0.06/0.12 mg/L for Gram-positive bacteria (Table 2).
- Eravacycline was more active than other tetracyclines tested, with MIC₉₀ values 8-fold lower than tigecycline against *A. baumannii* and 2- to 4-fold lower than tigecycline against *Enterobacteriaceae* isolates, respectively (Table 1).
- Similarly, eravacycline MIC₉₀ values were 4-fold or 8-fold lower than tigecycline against enterococci, MRSA or MSSA and 2-fold lower against *S. agalactiae*. Resistance to minocycline and tetracycline was high in *S. agalactiae* (Table 2).
- MDR in Gram-negative bacteria had no effect on the activity of eravacycline (Table 3).

Table 3. Susceptibility of multidrug-resistant (MDR) Gram-negative isolates to Eravacycline

Organism	MDR Gastrointestinal isolates					MDR Genitourinary isolates				
	N	MIC ₅₀	MIC ₉₀	MIN	MAX	N	MIC ₅₀	MIC ₉₀	MIN	MAX
<i>Acinetobacter baumannii</i>	24	0.5	1	0.5	2	25	1	1	0.5	1
<i>Escherichia coli</i>	4	-	-	0.12	0.25	22	0.12	0.5	0.06	2
<i>Klebsiella pneumoniae</i>	16	0.5	1	0.12	16	29	0.5	2	0.12	8
<i>Enterobacter cloacae</i>	11	0.5	1	0.25	4	11	0.5	-	0.25	1

Conclusions

Eravacycline demonstrated potent *in vitro* activity against a variety of clinically important Gram-negative and Gram-positive organisms from GU or GI sources, including MDR isolates.

References

- CLSI, 2015. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard - Tenth Edition M07-A10. CLSI, Wayne, PA 19087-1898 USA
- The European Committee on Antimicrobial Susceptibility testing, 2017. Breakpoint tables for interpretation of MICs and zone diameters. Version 7.1 <http://www.eucast.org>

Acknowledgments

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