

# P0099 *In vitro* activity of eravacycline and comparators against resistant Gram-negative isolates collected in 2016 from patients in Europe



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## Introduction

Eravacycline is a novel, fully-synthetic, fluorocycline antibiotic that is currently under review by the EMA and FDA for the treatment of complicated intra-abdominal infections.

This study evaluated the *in vitro* activity of eravacycline and comparators against *Enterobacteriaceae* and *Acinetobacter baumannii* isolates (including resistant strains) collected in 2016 from patients in Europe.

## Methods & Materials

Clinical isolates were collected in 2016 from hospitals in 14 European countries (Figure 1). Of the 1445 isolates, 207 were *A. baumannii* and 1,238 were *Enterobacteriaceae* (Figure 2).

MICs were determined against 1445 isolates for eravacycline and comparators by CLSI broth microdilution methodology (1).

ESBL-positivity was defined phenotypically according to CLSI guidelines (1) for selected *Enterobacteriaceae* organisms (*Klebsiella pneumoniae*, *K. oxytoca*, *Escherichia coli* & *Proteus mirabilis*).

3rd/4th cephalosporin resistance was defined as resistance to any one of the following: ceftriaxone, cefotaxime, ceftazidime or cefepime.

Carbapenem resistance was defined as resistant to meropenem or ertapenem.

Antibiotic susceptibility was determined using EUCAST breakpoints, where available (2).

## Results

Figure 1. Percent Distribution of All Isolates (n = 1,445) by European Country

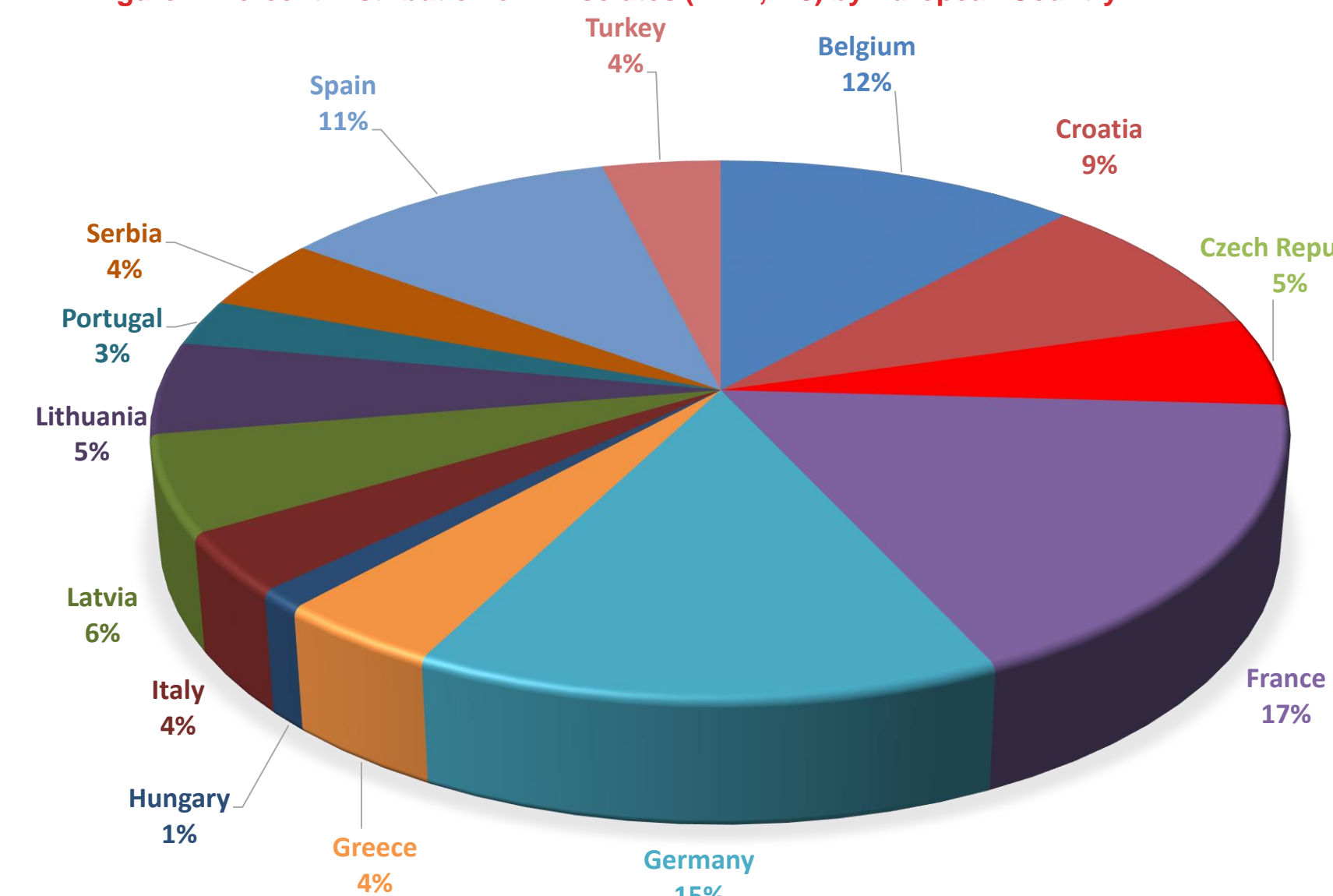


Figure 2. Distribution of *Enterobacteriaceae* by species

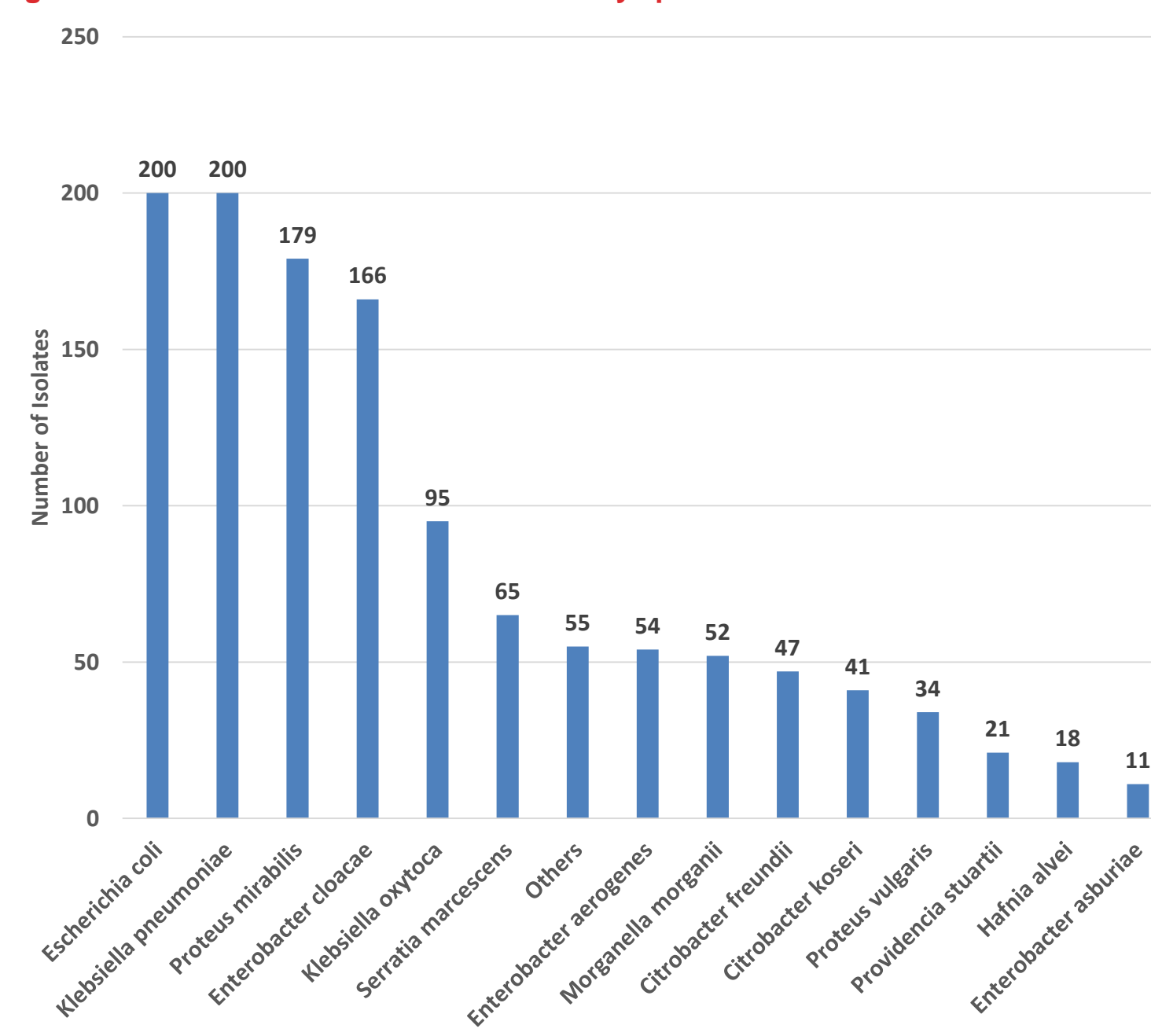


Table 1. Susceptibility of *A. baumannii* (n = 207) to Eravacycline and Comparators

Drug	Breakpoints (S I R)	%S	%I	%R	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amikacin	≤8   16   ≥32	36.2	1.9	61.8	>64	>64	0.25	>64
Ampicillin Sulbactam	NB	NB	NB	NB	64	>64	2	>64
Aztreonam	NB	NB	NB	NB	64	>64	≤0.03	>64
Cefepime	NB	NB	NB	NB	>64	>64	≤0.03	>64
Cefotaxime	NB	NB	NB	NB	>64	>64	0.12	>64
Ceftazidime	NB	NB	NB	NB	>64	>64	≤0.03	>64
Ceftriaxone	NB	NB	NB	NB	>64	>64	≤0.03	>64
Colistin	≤2   --   ≥4	99.0	0.0	1.0	0.5	0.5	0.25	>32
<b>Eravacycline</b>	<b>NB</b>	<b>0.5</b>	<b>1</b>	<b>0.03</b>	<b>8</b>			
Gentamicin	≤4   --   ≥8	25.6	0.0	74.4	>64	>64	0.25	>64
Levofloxacin	≤0.5   1   ≥2	15.0	0.5	84.5	16	>64	0.06	>64
Meropenem	≤2   4-8   ≥16	19.8	1.5	78.7	64	>64	≤0.03	>64
Minocycline	NB	NB	NB	NB	8	16	0.12	32
Piperacillin Tazobactam	NB	NB	NB	NB	>128	>128	≤0.06	>128
Tetracycline	NB	NB	NB	NB	>64	>64	1	>64
Tigecycline	NB	NB	NB	NB	4	8	0.25	>16

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

Table 2. Susceptibility of carbapenem-resistant *A. baumannii* (n = 163) to Eravacycline and Comparators

Drug	Breakpoints (S I R)	%S	%I	%R	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amikacin	≤8   16   ≥32	29.5	2.5	68.1	>64	>64	0.25	>64
Ampicillin Sulbactam	NB	NB	NB	NB	64	>64	8	>64
Aztreonam	NB	NB	NB	NB	>64	>64	16	>64
Cefepime	NB	NB	NB	NB	>64	>64	8	>64
Ceftazidime	NB	NB	NB	NB	>64	>64	4	>64
Ceftriaxone	NB	NB	NB	NB	>64	>64	8	>64
Colistin	≤2   --   ≥4	98.8	0.0	1.2	0.5	0.5	0.25	>32
<b>Eravacycline</b>	<b>NB</b>	<b>0.5</b>	<b>1</b>	<b>0.12</b>	<b>8</b>			
Gentamicin	≤4   --   ≥8	19.6	0.0	80.4	>64	>64	0.25	>64
Levofloxacin	≤0.5   1   ≥2	0.0	0.6	99.4	16	>64	1	>64
Meropenem	≤2   4-8   ≥16	0.0	0.0	100.0	>64	>64	16	>64
Minocycline	NB	NB	NB	NB	8	16	0.5	32
Piperacillin Tazobactam	NB	NB	NB	NB	>128	>128	128	>128
Tetracycline	NB	NB	NB	NB	>64	>64	8	>64
Tigecycline	NB	NB	NB	NB	4	8	1	>16

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

Table 3. Susceptibility of All *Enterobacteriaceae* (n = 1,238) to Eravacycline and Comparators

Drug	Breakpoints (S I R)	%S	%I	%R	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amikacin	≤8   16   ≥32	95.7	1.3	3.0	1	4	≤0.25	>64
Aztreonam	≤1   2-4   ≥8	78.0	3.6	18.5	0.12	>16	≤0.03	>16
Cefepime	≤1   2-4   ≥8	82.9	3.3	13.8	0.06	>16	≤0.008	>16
Cefotaxime	≤1   2   ≥4	73.4	1.8	24.8	0.12	>64	≤0.015	>64
Ceftazidime	≤1   2-4   ≥8	76.2	2.8	21.0	0.12	64	≤0.03	>128
Ceftriaxone	≤1   2   ≥4	73.1	1.1	25.8	0.12	>4	≤0.015	>4
<b>Eravacycline</b>	<b>NB</b>	<b>0.25</b>	<b>2</b>	<b>0.06</b>	<b>16</b>			
Ertapenem	≤0.5   1   ≥2	94.8	2.2	3.0	0.015	0.25	0.004	>2
Gentamicin	≤2   4   ≥8	84.1	1.5	14.4	0.5	>16	≤0.12	>16
Levofloxacin	≤0.5   1   ≥2	76.1	4.8	19.1	0.06	8	0.008	>8
Meropenem	≤2   4-8   ≥16	98.7	1.3	0.0	0.06	0.12	0.015	>4
Minocycline	NB	NB	NB	NB	4	>16	0.25	>16
Piperacillin Tazobactam	≤8   16   ≥32	79.2	6.8	14.0	2	64	≤0.25	>128
Tetracycline	NB	NB	NB	NB	4	>64	0.5	>64
Tigecycline	≤1   2   ≥4	69.6	15.1	15.3	0.5	4	0.03	16

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

Table 4. Susceptibility of carbapenem-resistant *Enterobacteriaceae* (n = 37) to Eravacycline and Comparators

Drug	Breakpoints (S I R)	%S	%I	%R	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amikacin	≤8   16   ≥32	75.7	5.4	18.9	2	32	0.5	>64
Aztreonam	≤1   2-4   ≥8	10.8	0.0	89.2	>16	>16	0.06	>16
Cefepime	≤1   2-4   ≥8	35.1	2.7	62.2	>16	>16	0.06	>16
Cefotaxime	≤1   2   ≥4	8.1	0.0	91.9	>64	>64	0.5	>64
Ceftazidime	≤1   2-4   ≥8	8.1	2.7	89.2	128	>128	0.25	>128
Ceftriaxone	≤1   2   ≥4	8.1	0.0	91.9	>4	>4	0.5	>4
<b>Eravacycline</b>	<b>NB</b>	<b>0.5</b>	<b>2</b>	<b>0.12</b>	<b>16</b>			
Ertapenem	≤0.5   1   ≥2	0.0	0.0	100.0	>2	>2	2	>2
Gentamicin	≤2   4   ≥8	62.2	0.0	37.8	0.5	>16	0.25	>16
Levofloxacin	≤0.5   1   ≥2	24.3	18.9	56.8	4	>8	0.015	>8
Meropenem	≤2   4-8   ≥16	59.5	40.5	0.0	2	>4	0.06	>4
Minocycline	NB	NB	NB	NB	8	>16	0.5	>16
Piperacillin Tazobactam	≤8   16   ≥32	2.7	8.1	89.2	>128	>128	4	>128
Tetracycline	NB	NB	NB	NB	8	>64	0.5	>64
Tigecycline	≤1   2   ≥4	62.2	27.0	10.8	1	4	0.25	8

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

Table 5. Susceptibility of 3rd/4th generation cephalosporin-resistant *Enterobacteriaceae* (n = 343) to Eravacycline and Comparators

Drug	Breakpoints (S I R)	%S	%I	%R	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amikacin	≤8   16   ≥32	86.3	2.9	10.8	2	32	≤0.25	>64
Aztreonam	≤1   2-4   ≥8	22.5	11.1	66.5	>16	>16	≤0.03	>16
Cefepime	≤1   2-4   ≥8	39.4	10.8	49.9	4	>16	0.015	>16
Cefotaxime	≤1   2   ≥4	8.5	2.0	89.5	>64	>64	≤0.015	>64
Ceftazidime	≤1   2-4   ≥8	16.9	7.3	75.8	32	>128	≤0.03	>128
Ceftriaxone	≤1   2   ≥4	5.0	2.0	93.0	>4	>4	0.03	>4
<b>Eravacycline</b>	<b>NB</b>	<b>0.5</b>	<b>2</b>	<b>0.06</b>	<b>16</b>			
Ertapenem	≤0.5   1   ≥2	82.2	7.9	9.9	0.12	1	0.008	>2
Gentamicin	≤2   4   ≥8	54.5	2.3	43.2	2	>16	≤0.12	>16
Levofloxacin	≤0.5   1   ≥2	50.2	7.9	42.0	0.5	>8	0.015	>8
Meropenem	≤2   4-8   ≥16	95.6	4.4	0.0	0.12	0.5	0.015	>4
Minocycline	NB	NB	NB	NB	8	>16	0.5	>16
Piperacillin Tazobactam	≤8   16   ≥32	40.5	16.3	43.2	16	>128	≤0.25	>128
Tetracycline	NB	NB	NB	NB	16	>64	0.5	>64
Tigecycline	≤1   2   ≥4	61.8	19.8	18.4	1	4	0.12	16

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

Table 6. Susceptibility of ESBL-Positive *Enterobacteriaceae* (n = 118) to Eravacycline and Comparators

Drug	Breakpoints (S I R)	%S	%I	%R	MIC <sub>50</sub>	MIC <sub>90</sub>	MIN	MAX
Amikacin	≤8   16   ≥32	85.6	3.4	11.0	4	32	≤0.25	>64
Aztreonam	<=1   2-4   ≥8	7.6	10.2	82.2	>16	>16	<=0.03	>16
Cefepime	<=1   2-4   ≥8	0.9	11.9	87.3	>16	>16	0.25	>16
Cefotaxime	<=1   2   ≥4	0.0	0.9	99.2	>64	>64	2	>64
Ceftazidime	<=1   2-4   ≥8	13.6	5.9	80.5	64	>128	0.06	>128
Ceftriaxone	<=1   2   ≥4	0.0	0.9	99.2	>4	>4	2	>4
<b>Eravacycline</b>	<b>NB</b>	<b>0.5</b>	<b>2</b>	<b>0.06</b>	<b>16</b>			
Ertapenem	<=0.5   1   ≥2	83.1	7.6	9.3	0.12	1	0.008	>2
Gentamicin	<=2   4   ≥8	29.7	2.5	67.8	>16	>16	<=0.12	>16
Levofloxacin	<=0.5   1   ≥2	26.3	11.0	62.7	8	>8	0.03	>8
Meropenem	<=2   4-8   ≥16	94.9	5.1	0.0	0.06	0.25	0.03	>4
Minocycline	NB	NB	NB	NB	8	>16	0.5	>16
Piperacillin Tazobactam	<=8   16   ≥32	37.3	17.0	45.8	16	>128	<=0.25	>128
Tetracycline	NB	NB	NB	NB	>64	>64	0.5	>64
Tigecycline	<=1   2   ≥4	67.0	16.1	17.0	1	4	0.12	8

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

## Results Summary

- Eravacycline MIC<sub>90</sub> values were 1 and 2 mg/L for *A. baumannii* and *Enterobacteriaceae*, and were unaffected by resistance to other antibiotics.
- In addition, eravacycline MIC<sub>90</sub> values were 8-fold and 2-fold lower than tigecycline for *A. baumannii* and *Enterobacteriaceae* isolates, respectively.
- Resistance in *Enterobacteriaceae* was 3% – 18.5% for aminoglycosides, 13.8% – 25.8% for cephalosporins, 15.3% for tigecycline and 19.1% for levofloxacin. Most were carbapenem-susceptible.

## Conclusions

Eravacycline demonstrated potent *in vitro* activity against these resistant Gram-negative organisms isolated from European patients.

## References