Surveillance of the *in vitro* activity of eravacycline and comparators against clinical isolates from the USA from 2013 - 2016

Samuel Bouchillon[1], Stephen Hawser[2], Federica Monti[2],

Ian Morrissey[2], Kristen Ditch[3],

Melanie Olesky[3], Corey Fyfe[3]

[1]IHMA, Inc., Schaumburg, IL

[2]IHMA Europe, Monthey, Switzerland

[3]Tetraphase Pharmaceuticals, Watertown, MA

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Disclosures

- KD, MO, CF are employees of Tetraphase Pharmaceuticals
- SB is employed by IHMA, Inc
- SH, IM, FM are employees of IHMA Europe
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Background

- Eravacycline is a novel, fully-synthetic fluorocycline antibiotic that has completed phase 3 clinical development for patients with complicated intra-abdominal infection (cIAI) and is currently under regulatory review with the FDA and EMA.
- The present surveillance study monitored the *in vitro* activity of eravacycline and comparators against clinical isolates from patients in the United States isolated during 2013-2016.

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Methods

- A total of 7,815 non-duplicate, non-consecutive, single-patient clinical isolates were collected during 2013- 2016 from hospitals throughout the United States.
- These comprised *Enterobacteriaceae* (n = 5,142), *Acinetobacter baumannii* (n = 717) and Gram-positive isolates (n = 1,956).
- Isolates were from multiple infection sources, including blood, body fluids, gastrointestinal, genitourinary, skin, and respiratory.
- MICs were determined by CLSI broth microdilution. Tigecycline susceptibility was interpreted using FDA breakpoints.

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Activity of Eravacycline and Selected Comparators Against Gram-Positive Pathogens

	Drug	Breakpoints (S|I|R)	N	MIC_{50}	MIC_{90}	Min	Max	%S	%I	%R
***Staphylococcus aureus*, MRSA**	Eravacycline	No Breakpoints Defined	546	0.06	0.12	0.015	1	-	-	-
	Linezolid	≤4 | -- | ≥8	546	2	2	<= 0.5	2	100.0	0.0	0.0
	Tigecycline	≤0.5 | - | - *	546	0.12	0.25	0.03	2	98.4	0.0	1.7
	Vancomycin	≤2 | 4-8 | ≥16	204	1	1	0.5	2	100.0	0.0	0.0
***Staphylococcus aureus*, MSSA**	Eravacycline	No Breakpoints Defined	555	0.06	0.12	<= 0.008	0.5	-	-	-
	Linezolid	≤4 | -- | ≥8	555	2	2	<= 0.5	2	100.0	0.0	0.0
	Tigecycline	≤0.5 | - | - *	555	0.12	0.25	0.03	1	99.6	0.0	0.4
	Vancomycin	≤2 | 4-8 | ≥16	215	1	1	0.5	2	100.0	0.0	0.0
Enterococcus faecalis	Eravacycline	No Breakpoints Defined	482	0.06	0.06	0.008	0.5	-	-	-
	Ampicillin	≤8 | -- | ≥16	129	1	2	0.5	> 8	99.2	0.0	0.8
	Linezolid	≤2 | 4 | ≥8	482	2	2	<= 0.5	4	99.4	0.6	0.0
	Tigecycline	≤0.25 | -- | --*	482	0.12	0.25	<= 0.015	1	98.1	0.0	1.9
	Vancomycin	≤4 | 8-16 | ≥32	481	1	2	0.12	> 32	92.5	0.2	7.3
Enterococcus faecium	Eravacycline	No Breakpoints Defined	368	0.06	0.06	0.008	0.5	-	-	-
	Ampicillin	≤8 | -- | ≥16	60	> 8	> 8	0.5	> 8	15.0	0.0	85.0
	Linezolid	≤2 | 4 | ≥8	368	2	2	<= 0.5	> 8	97.8	1.4	0.8
	Tigecycline	≤0.25 | -- | --*	368	0.12	0.25	0.03	1	93.2	0.0	6.8
	Vancomycin	≤4 | 8-16 | ≥32	366	> 32	> 32	<= 0.25	> 32	26.8	0.8	72.4

* FDA breakpoint

Activity of Eravacycline and Selected Comparators Against Gram-Negative pathogens

	Drug	Breakpoints (S|I|R)	N	MIC_{50}	MIC_{90}	Min	Max	%S	%I	%R
Enterobacteriaceae	Eravacycline	No Breakpoints Defined	5142	0.25	2	0.03	8	-	-	-
	Cefepime	≤2 | 4-8 | ≥16	5142	<= 0.25	1	<= 0.008	> 16	93.4	2.6	4.0
	Ceftriaxone	≤1 | 2 | ≥4	5142	<= 0.5	> 4	<= 0.015	> 32	83.2	1.3	15.6
	Meropenem	≤1 | 2 | ≥4	2419	0.03	0.06	<= 0.004	> 4	98.3	0.2	1.5
	Piperacillin Tazobactam	≤16/4 | 32/4-64/4 | ≥128/4	5142	2	32	<= 0.25	> 128	88.6	7.0	4.4
	Tigecycline	≤2 | 4 | ≥8 *	5142	0.5	4	0.03	32	90.0	7.5	2.5
***Enterobacter* spp.**	Eravacycline	No Breakpoints Defined	1268	0.5	0.5	0.06	8	-	-	-
	Cefepime	≤2 | 4-8 | ≥16	1268	<= 0.25	2	0.015	> 16	93.61	4.65	1.74
	Ceftriaxone	≤1 | 2 | ≥4	1268	<= 0.5	32	<= 0.015	> 32	71.14	1.42	27.44
	Meropenem	≤1 | 2 | ≥4	569	0.03	0.12	0.008	> 4	98.95	0.53	0.53
	Piperacillin Tazobactam	≤16/4 | 32/4-64/4 | ≥128/4	1268	4	64	<= 0.25	> 128	78.15	16.17	5.68
	Tigecycline	≤2 | 4 | ≥8 *	1268	0.5	1	0.03	8	95.98	3	1.03
Escherichia coli	Eravacycline	No Breakpoints Defined	761	0.12	0.25	0.03	2	-	-	-
	Cefepime	≤2 | 4-8 | ≥16	761	<= 0.25	8	<= 0.008	> 16	86.7	3.4	9.9
	Ceftriaxone	≤1 | 2 | ≥4	761	<= 0.5	> 4	<= 0.015	> 32	84.2	0.1	15.6
	Meropenem	≤1 | 2 | ≥4	412	0.03	0.03	0.008	2	99.8	0.2	0.0
	Piperacillin Tazobactam	≤16/4 | 32/4-64/4 | ≥128/4	761	2	8	<= 0.25	> 128	93.0	4.6	2.4
	Tigecycline	≤2 | 4 | ≥8 *	761	0.25	0.5	0.06	4	99.0	1.1	0.0
***Klebsiella* spp.**	Eravacycline	No Breakpoints Defined	1388	0.25	1	0.06	8	-	-	-
	Cefepime	≤2 | 4-8 | ≥16	1388	<= 0.25	1	<= 0.008	> 16	93.0	1.4	5.6
	Ceftriaxone	≤1 | 2 | ≥4	1388	<= 0.5	4	<= 0.015	> 32	89.1	0.7	10.2
	Meropenem	≤1 | 2 | ≥4	691	0.03	0.06	<= 0.004	> 4	97.4	0.1	2.5
	Piperacillin Tazobactam	≤16/4 | 32/4-64/4 | ≥128/4	1388	2	16	<= 0.25	> 128	90.4	4.0	5.6
	Tigecycline	≤2 | 4 | ≥8*	1388	0.5	2	0.06	16	95.5	3.8	0.7
Acinetobacter baumannii	Eravacycline	No Breakpoints Defined	717	0.5	2	<= 0.015	16	-	-	-
	Cefepime	≤8 | 16 | ≥32	717	16	64	<= 0.25	> 64	35.01	16.46	48.54
	Ceftriaxone	≤8 | 16-32 | ≥64	717	> 32	> 64	<= 0.5	> 64	17.02	22.59	60.39
	Meropenem	≤2 | 4 | ≥8	368	8	> 64	0.06	> 64	46.2	3.26	50.54
	Piperacillin Tazobactam	≤16/4 | 32/4-64/4 | ≥128/4	717	> 64	> 128	<= 0.06	> 128	31.8	8.51	59.69
	Tigecycline	No Breakpoints Defined*	717	2	4	0.06	> 16	-	-	-

* FDA breakpoint

Conclusions

- Eravacycline exhibited potent antibacterial activity against the vast majority of isolates, irrespective of infection source origin.
- Eravacycline was 2- to 4-fold more active than tigecycline against both Gram-negative and Gram-positive clinical isolates.
- Eravacycline completed two phase 3 trials for the treatment of cIAI demonstrating non-inferiority to ertapenem and meropenem, and is currently under regulatory review.

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