Eravacycline

ANTONIO VENA

Clinical Infectious Diseases

University of Genoa

San Martino Polyclinic Hospital- Genoa, Italy

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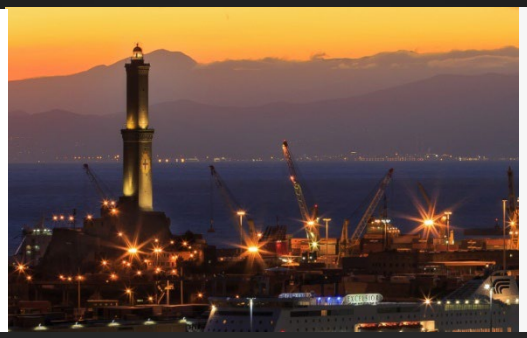

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Conflict of interest

Nothing to declare.

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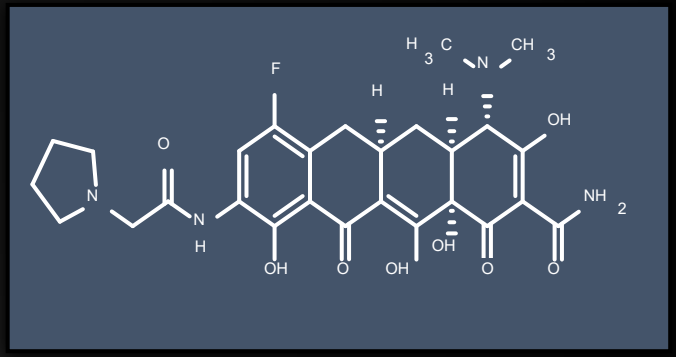
1- The drug

Pharmacology
Eravacycline (30s rRNA)

- Novel, fully-synthetic fluorocycline antibacterial for intravenous administration



- Retains activity against the most common tetracycline-specific acquired resistance mechanisms (i.e., efflux and ribosomal protection)

- Broad spectrum activity against certain Gram-negative, Gram-positive and anaerobic organisms

Newman JV et al. Antimicrob Agents Chemother. 2019
XERAVA™ (eravacycline) Summary of Product Characteristics PAION 2023

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Spectrum of activity

GOOD IN VITRO ACTIVITY

- *Enterobacterales*
- *Acinetobacter* spp
- *S. malthophilia*
- *Staphylococcus aureus*
- *Enterococcus* spp
- *Viridans Streptococcus* spp
- **Anaerobes**
- Chlamydophila and Mycoplasma
- *H. influenzae*
- *Legionella* spp

Pseudomonas aeruginosa

Proteus spp.
Serratia spp.
Providencia spp.
Morganella spp

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Proprierties of Eravacycline

CHARACTERISTICS	
FDA /EMA Dosing approved	1 mg/kg every 12 hours for 4 to 14 days.
Infusion time	1 hour
C_{max}	1,825 (multiple 1 mg/kg q 12h dose)
Renal dose adjustment	No dose adjustment (even in patients undergoing HD).
Hepatic dose adjustment	Not required
Drug-drug interactions	In patients co-administered strong CYP3A4 inducers the recommended dose regimen is 1.5 mg/kg every 12 h for 4 to 14 days

1. Xerava 100mg. Summary of Product Characteristics. 2022. Available at: https://www.medicines.org.uk/emc/product/13327 – Accessed February 2023

2- Clinical studies

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JAMA Surgery | Original Investigation

Assessing the Efficacy and Safety of Eravacycline vs Ertapenem in Complicated Intra-abdominal Infections in the Investigating Gram-Negative Infections Treated With Eravacycline (IGNITE 1) Trial

A Randomized Clinical Trial

Joseph Solomkin, MD; David Evans, MD; Algirdas Slepavicius, MD; Patrick Lee, MD; Andrew Marsh; Larry Tsai, MD; Joyce A. Sutcliffe, PhD; Patrick Horn, MD

Solomkin J, Evans D, Slepavicius A, et al. JAMA Surg. 2017;152(3):224-232.

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

IGNITE4: Results of a Phase 3, Randomized, Multicenter, Prospective Trial of Eravacycline vs Meropenem in the Treatment of Complicated Intraabdominal Infections

Joseph S. Solomkin,[1] Janis Gardovskis,[2] Kenneth Lawrence,[3] Philippe Montravers,[4,5,6] Angie Sway,[7] David Evans,[8] and Larry Tsai[3]

[1]Department of Surgery, University of Cincinnati College of Medicine, Ohio; [2]Department of Surgery, Riga Stradins University, Latvia; [3]Tetraphase Pharmaceuticals, Watertown, Massachusetts; [4]Département d'Anesthésie-Réanimation, CHU Bichat Claude Bernard [5]Université Paris Diderot, PRESS Sorbonne Cité, and [6]Institut National de la Santé et de la Recherche Médicale (INSERM) UMR 1152, Paris, France; and [7]World Surgical Infection Society, Cincinnati, Ohio and [8]Department of Surgery, Ohio State University School of Medicine, Columbus

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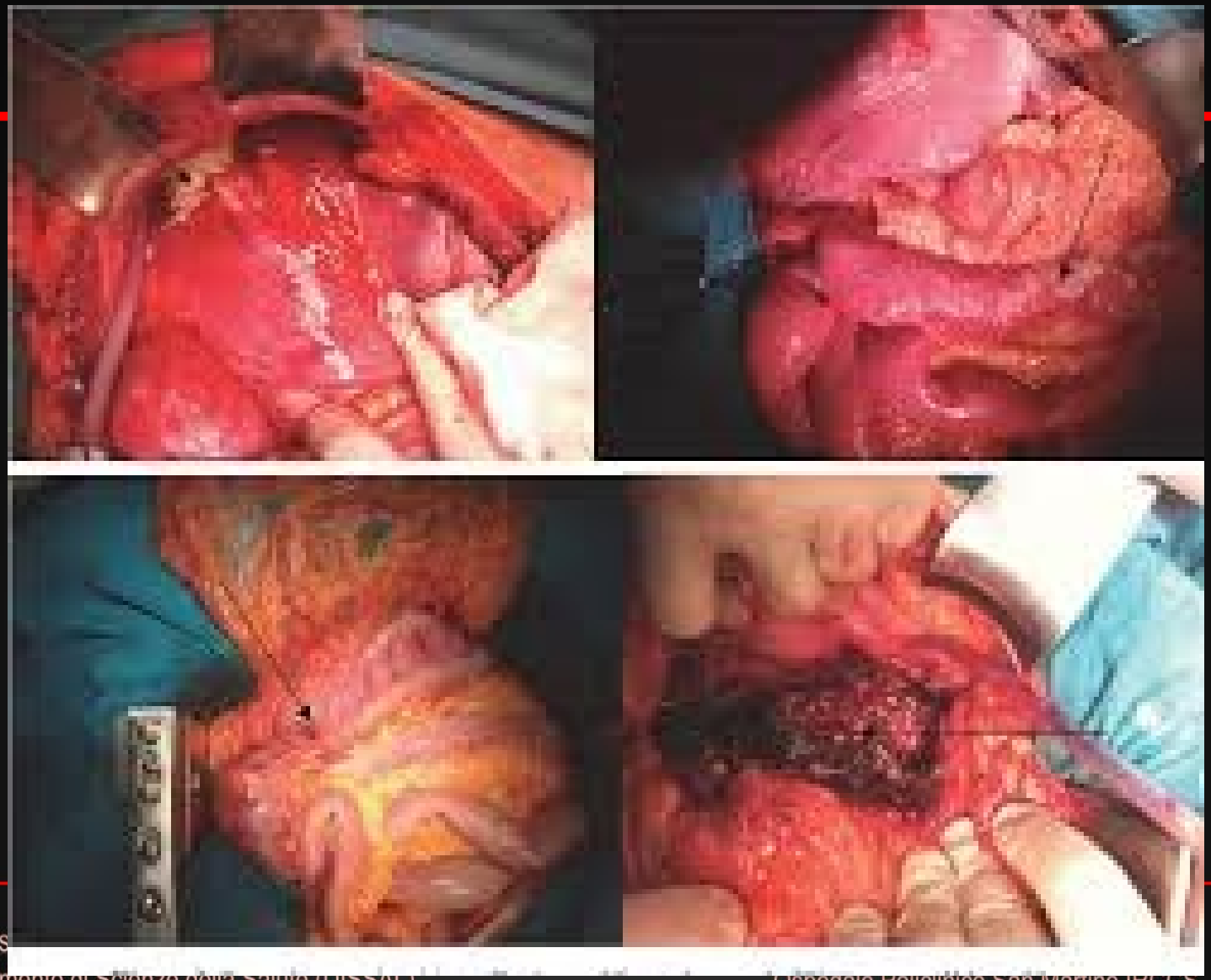

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Empirical and targeted treatment for cIAI

Sartelli *et al.*
World Journal of Emergency Surgery (2024) 19:23
https://doi.org/10.1186/s13017-024-00551-w

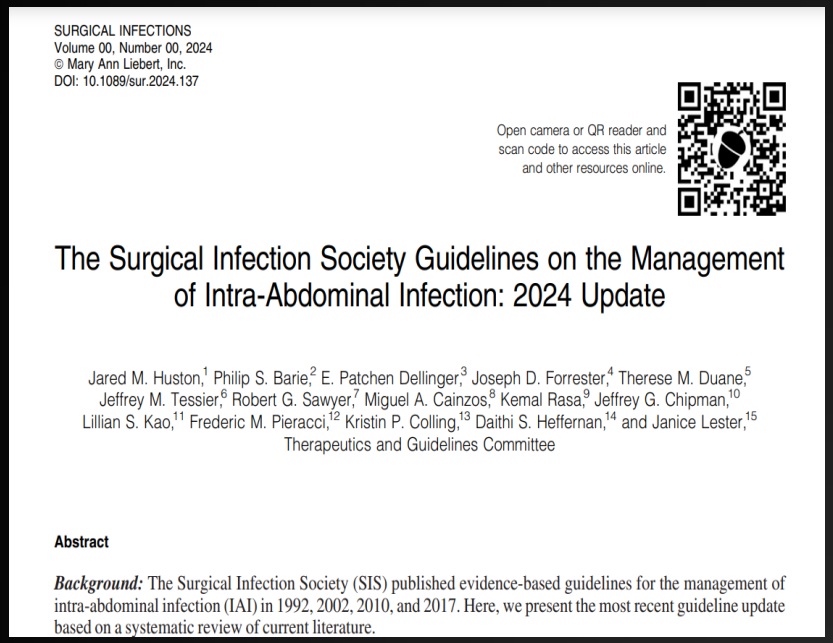
World Journal of Emergency Surgery

REVIEW Open Access

Management of intra-abdominal infections: recommendations by the Italian council for the optimization of antimicrobial use

Massimo Sartelli[1*], Carlo Tascini[2,3], Federico Coccolini[4], Fabiana Dellai[3], Luca Ansaloni[5,6], Massimo Antonelli[7,8], Michele Bartoletti[9,10], Matteo Bassetti[11,12], Federico Boncagni[13], Massimo Carlini[14], Anna Maria Cattelan[15,16], Arturo Cavaliere[17], Marco Ceresoli[18], Alessandro Cipriano[19], Andrea Cortegiani[20,21], Francesco Cortese[22], Francesco Cristini[23,24], Eugenio Cucinotta[25], Lidia Dalfino[26], Gennaro De Pascale[7,8], Francesco Giuseppe De Rosa[27], Marco Falcone[28], Francesco Forfori[29], Paola Fugazzola[5,6], Milo Gatti[30,31], Ivan Gentile[32], Lorenzo Ghiadoni[19,33], Maddalena Giannella[30,34], Antonino Giarratano[20,21], Alessio Giordano[35], Massimo Girardis[36], Claudio Mastroianni[37], Gianpaola Monti[38], Giulia Montori[39], Miriam Palmieri[1], Marcello Pani[40], Ciro Paolillo[41], Dario Parini[42], Giustino Parruti[43], Daniela Pasero[44,45], Federico Pea[30,31], Maddalena Peghin[46], Nicola Petrosillo[47], Mauro Podda[48], Caterina Rizzo[49], Gian Maria Rossolini[50,51], Alessandro Russo[52,53], Loredana Scoccia[54], Gabriele Sganga[55,56], Liana Signorini[57], Stefania Stefani[58], Mario Tumbarello[59,60], Fabio Tumietto[61], Massimo Valentino[62], Mario Venditti[63], Bruno Viaggi[64], Francesca Vivaldi[65], Claudia Zaghi[66], Francesco M. Labricciosa[67], Fikri Abu-Zidan[68], Fausto Catena[69] and Pierluigi Viale[30,34]

Empirical treatment



SURGICAL INFECTIONS
Volume 00, Number 00, 2024

DOI: 10.1089/sur.2024.137

Open camera or QR reader and scan code to access this article and other resources online.

The Surgical Infection Society Guidelines on the Management of Intra-Abdominal Infection: 2024 Update

Jared M. Huston,[1] Philip S. Barie,[2] E. Patchen Dellinger,[3] Joseph D. Forrester,[4] Therese M. Duane,[5] Jeffrey M. Tessier,[6] Robert G. Sawyer,[7] Miguel A. Cainzos,[8] Kemal Rasa,[9] Jeffrey G. Chipman,[10] Lillian S. Kao,[11] Frederic M. Pieracci,[12] Kristin P. Colling,[13] Daithi S. Heffernan,[14] and Janice Lester,[15] Therapeutics and Guidelines Committee

Abstract

Background: The Surgical Infection Society (SIS) published evidence-based guidelines for the management of intra-abdominal infection (IAI) in 1992, 2002, 2010, and 2017. Here, we present the most recent guideline update based on a systematic review of current literature.

SIS GUIDELINES ON THE MANAGEMENT OF IAI

- We recommend eravacycline for empiric therapy (Grade 1-A).
- *"We suggest reserving eravacycline for higher risk patients due to its broader spectrum antimicrobial agent activity (Grade 2-C). These new recommendations are based on two doubleblind RCTs, four meta-analyses, and two systematic reviews and meta-analyses, totaling 1,080 patients with IAI treated with eravacycline versus comparator agents, including ertapenem or meropenem. Overall, the systemic reviews and meta-analyses found similar clinical efficacy of eravacycline versus comparators"*

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3- Real life experiences

AMERICAN SOCIETY FOR MICROBIOLOGY | Microbiology Spectrum

| Antimicrobial Chemotherapy | Research Article

Eravacycline, the first four years: health outcomes and tolerability data for 19 hospitals in 5 U.S. regions from 2018 to 2022

Ashlan J. Kunz Coyne,[1] Sara Alosaimy,[1] Kristen Lucas,[1] Abdalhamid M. Lagnf,[1] Taylor Morrisette,[1] Kyle C. Molina,[2] Alaina DeKerlegand,[3] Melanie Rae Schrack,[3] S. Lena Kang-Birken,[4] Athena L.V. Hobbs,[5] Jazmin Agee,[5] Nicholson B. Perkins III,[5] Mark Biagi,[6,7] Michael Pierce,[6] James Truong,[8] Justin Andrade,[9] Jeannette Bouchard,[10] Tristan Gore,[10] Madeline A. King,[11,12] Benjamin M. Pullinger,[11] Kimberly C. Claeys,[13] Shelbye Herbin,[14] Reese Cosimi,[15] Serina Tart,[16] Michael P. Veve,[17,18] Bruce M. Jones,[19] Leonor M. Rojas,[20] Amy K. Feehan,[21,22] Marco R. Scipione,[23,24] Jing J. Zhao,[23,24] Paige Witucki,[1] Michael J. Rybak[1,24,25]

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Eravacycline, the first four years: health outcomes and tolerability data for 19 hospitals in 5 U.S. regions from 2018 to 2022

- **Primary outcome:** to assess the clinical impact, microb. outcomes, and AE associated with eravacycline

- **Results:** **416 pts**, CCI 4.5
  - Median duration of eravacycline therapy 6.9 days (IQR 4.1 to 11.9)
  - Combo Tx **50.7%** (n = 211)→ mero, AG, TMP/SFX

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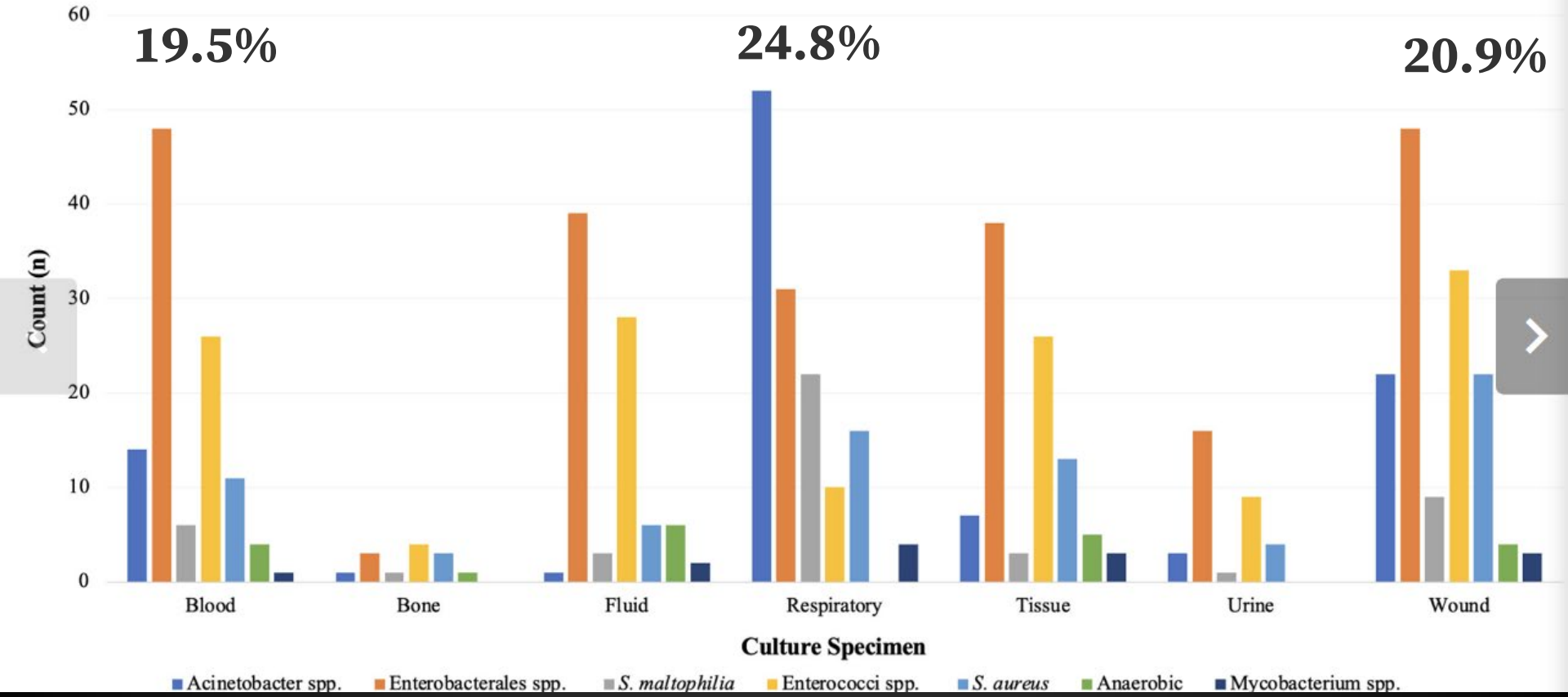
TABLE 3 Definitive eravacycline therapy

Parameter	Value
Gram-negative	
Achromobacter spp.	4 (1)
Acinetobacter spp.	97 (23.3)
Acinetobacter baumannii	92 (22.1)
Carbapenem-resistant *Acinetobacter* spp.	46 (11.1)
Enterobacterales	176 (42.3)
Citrobacter freundii	6 (1.4)
Enterobacter cloacae	33 (7.9)
Escherichia coli	50 (12)
Klebsiella aerogenes	5 (1.2)
Klebsiella oxytoca	12 (2.9)
Klebsiella pneumoniae	54 (13)
Morganella morganii	4 (1)
Proteus mirabilis	5 (1.2)
Proteus vulgaris	1 (0.2)
Providencia stuartii	3 (0.7)
Serratia marcescens	3 (0.7)
Carbapenem-resistant Enterobacterales	43 (10.3)
Pseudomonas aeruginosa	0 (0)
Stenotrophomonas maltophilia	41 (9.9)
Gram-positive	
Enterococci	100 (24)
Enterococcus faecalis	45 (10.8)
Enterococcus faecium	55 (13.2)
Vancomycin-resistant enterococci	49 (11.8)
Staphylococcus aureus	51 (12.3)
MRSA	48 (11.5)
Coagulase negative staphylococci	14 (3.4)
Streptococcus spp.	18 (4.3)
S. anginosus	9 (2.2)
Anaerobes	16 (3.8)
Bacteroides fragilis	6 (1.4)
Bacteroides ovatus	1 (0.2)
Bacteroides thetaiotaomicron	2 (0.5)
Clostridiodes difficile	7 (16.8)
Fungal	2 (0.5)
Mycobacterium spp.	
Mycobacterium abscessus	14 (3.4)
Polymicrobial	157 (37.7)

3 1 2

Specimens



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Outcomes

Clinical success occurred in 75.7% of patients (*n* = 315/416).

TEAE in 9.4% of patients, mainly gastrointestinal intolerance.

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Eravacycline

In which clinical context, do we believe the drug offers added value?

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Place in therapy

4- Tygecicline competitor

Global Surveillance: MDR Gram-negative Pathogens 2nd

Organism	N	ERV $MIC_{50/90}$	TGC $MIC_{50/90}$	MEM* $MIC_{50/90}$	PTZ $MIC_{50/90}$	AMK* $MIC_{50/90}$	FEP $MIC_{50/90}$
Acinetobacter baumannii	1,502	0.5/2	4/8	64/>64	>64/>64	>64/>64	>16/>16
Citrobacter spp.	247	0.25/1	0.5/2	0.06/1	>64/>64	1/8	2/>16
Enterobacter spp.	448	0.5/2	1/4	0.12/0.5	64/>64	1/4	4/>16
Escherichia coli	555	0.25/0.5	0.25/1	0.03/0.06	4/64	2/8	8/>16
Klebsiella spp.	801	0.5/2	1/4	0.06/>4	64/>64	2/16	>16/>16

Morrissey I, Olesky M, Hawser S, et al. Antimicrob Agents Chemother. 2019

Global Surveillance: MDR Gram-negative Pathogens 2nd

Eravacycline showed to be **four-to-eight times** more active than tigecycline

Organism	N	ERV $MIC_{50/90}$	TGC $MIC_{50/90}$	MEM* $MIC_{50/90}$	PTZ $MIC_{50/90}$	AMK* $MIC_{50/90}$	FEP $MIC_{50/90}$
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Klebsiella spp.	801	0.5/2	1/4	0.06/>4	64/>64	2/16	>16/>16

Morrissey I, Olesky M, Hawser S, et al. Antimicrob Agents Chemother. 2019

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Antimicrobial activity largely unaffected by common tetracycline resistance mechanisms

Eravacycline *in vitro* activity: tetracycline-specific resistance genotypes

	MIC (µg/ml) for *E. coli* strain expressing:					
Antibiotic	*lacZ*	*tet*(M)	*tet*(K)	*tet*(A)	*tet*(B)	*tet*(X)
Eravacycline	0.063	0.063	0.031	0.25	0.063	4
Tigecycline	0.063	0.13	0.063	1	0.063	2
Doxycycline	2	64	4	32	32	16
Minocycline	0.5	64	1	8	16	4
Tetracycline	2	128	128	>128	>128	128
Ceftriaxone	0.063	0.13	0.063	0.13	0.13	0.13

Tetracycline-specific efflux pumps

Grossman TH, et al. Antimicrob Agents Chemother. 2012;56(5):2559–64.

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No FDA warns for eravacycline

FDA Drug Safety Communication: FDA warns of increased risk of death with IV antibacterial Tygacil (tigecycline) and approves new Boxed Warning

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This update is in follow-up to the FDA Drug Safety Communication: Increased risk of death with Tygacil (tigecycline) compared to other antibiotics used to treat similar infections issued on September 1, 2010.

Safety Announcement

[9-27-2013] The U.S. Food and Drug Administration (FDA) is warning that an additional analysis shows an increased risk of death when intravenous (IV) Tygacil (tigecycline) is used for FDA-approved uses as well as for non-approved uses. As a result, we approved a new *Boxed Warning* about this risk to be added to the Tygacil drug label and updated the *Warnings and Precautions* and the *Adverse Reactions* sections. A *Boxed Warning* is the strongest warning given to a drug. These changes to the Tygacil label are based on an additional analysis that was conducted for FDA-approved uses after issuing a Drug Safety Communication (DSC) about this safety concern in September 2010.

1.FDA Drug Safety Communication: FDA warns of increased risk of death with IV antibacterial Tygacil (tigecycline) and approves new Boxed Warning

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IGNITE1-4 vs pooled analysis TIG trials

Type of AE	Eravacycline (N = 250)
Nausea	12 (4.8)
Vomitting	9 (3.6)
Infusion site phlebitis	8 (3.2)
Infusion site thrombosis	6 (2.4)
Wound infection (superficial)	7 (2.8)
Diarrhea	6 (2.4)
Anemia	3 (1.2)
Hypertension	2 (0.8)
Hypokalemia	0
Discontinued because of adverse event	4 (1.6)

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Babinchak T. CID 2005

Body system adverse event[a]	Tigecycline (*n* = 817)
Any	603 (73.8)
Body as a whole	289 (35.4)
Abdominal pain	65 (8.0)
Fever	74 (9.1)
Headache	28 (3.4)
Infection	83 (10.2)
Cardiovascular system	121 (14.8)
Hypertension	49 (6.0)
Phlebitis	16 (2.0)
Digestive system	363 (44.4)
Constipation	21 (2.6)
Diarrhea	113 (13.8)
Nausea	199 (24.4)
Vomiting	157 (19.2)
Hemic and lymphatic system	123 (15.1)
Anemia	39 (4.8)
Leukocytosis	36 (4.4)
Thrombocythemia	49 (6.0)
Metabolic and nutritional	215 (26.3)
Alkaline phosphatase increased	33 (4.0)
Healing abnormal	37 (4.5)
Hypokalemia	19 (2.3)
Hypoproteinemia	48 (5.9)
Lactate dehydrogenase increased	38 (4.7)
Peripheral edema	30 (3.7)
AST increased	24 (2.9)
ALT increased	27 (3.3)
Respiratory system	138 (16.9)

Place in therapy

5- Treatment of MDR pathogens

Place in therapy

5- Treatment of MDR pathogens

a) Gram positive

Activity of eravacycline against MDR Gram-positive pathogens

Pathogens	Study sites	No. of isolate	MIC50 (mg/L)	MIC90 (mg/L)	Susceptibility (%)FDA/EUCAST
MRSA					
Zhanel et al. 2018	Canada	301	0.06	0.12	NA
Zhang et al. 2018	China	138	0.25	0.5	NA
Zhao et al. 2019	China	15	0.25	0.5	NA
Morrissey et al. 2020	Multination	1304	0.06	0.12	80.8/95.5
Ding et al. 2022	China	541	0.06	0.25	76/92.1
Rolston et al. 2023	US	20	0.015	0.015	100/NA
Hawser et al. 2023	Multination	1030	0.03	0.12	82.7/97.6
Vancomycin-resistant E. faecium					
Morrissey et al. 2020	Multination	510	0.03	0.06	93.1/96.1
Ding et al. 2022	China	30	0.03	0.125	76.7/90.0
Rolston et al. 2023	US	20	0.06	0.25	85/NA
Hawser et al. 2023	Multination	588	0.03	0.06	92.4/96.9
Penicillin-non-susceptible *Streptococcus pneumoniae*					
Zhanel et al. 2018	Canada	10	0.008	0.015	NA
Zhao et al. 2019	China	10	0.008	0.008	NA
Hipp et al. 2019	Germany	56	0.008	0.012	NA

Management of vancomycin-resistant *Enterococci* and daptomycin-resistant *Enterococci* infections in liver transplant recipients in a single academic center

- 16 liver transplant patients treated with VRE for cIAI and BSI
- **Inadequate source control**: 70%
- **Breakthrough infection** in 63%
- **Death** during ERV 30%

Characteristic	Eravacycline use, N (%)
Preceding daptomycin use	12 (75%)
Type of positive culture[†]	
Blood	9 (56%)
Intraabdominal/peritoneal fluid	11 (69%)
Other	2 (13%)
Source control intervention	13 (31%)
Drain	5 (31%)
Reoperation	7 (43%)
Biliary stent	3 (19%)
Daptomycin resistance	6 (38%)
Timing of Initiation of ERV	
Initial therapy	4 (25%)
Breakthrough infection	10 (63%)
Recurrence	2 (13%)
Other indication[‡]	3 (19%)
Breakthrough infection on ERV	2 (13%)
Recurrent infection after ERV	1 (6%)
Death	8 (50%)
Expired on ERV	5 (31%)

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Place in therapy

5- Treatment of MDR pathogens

a) Gram positive

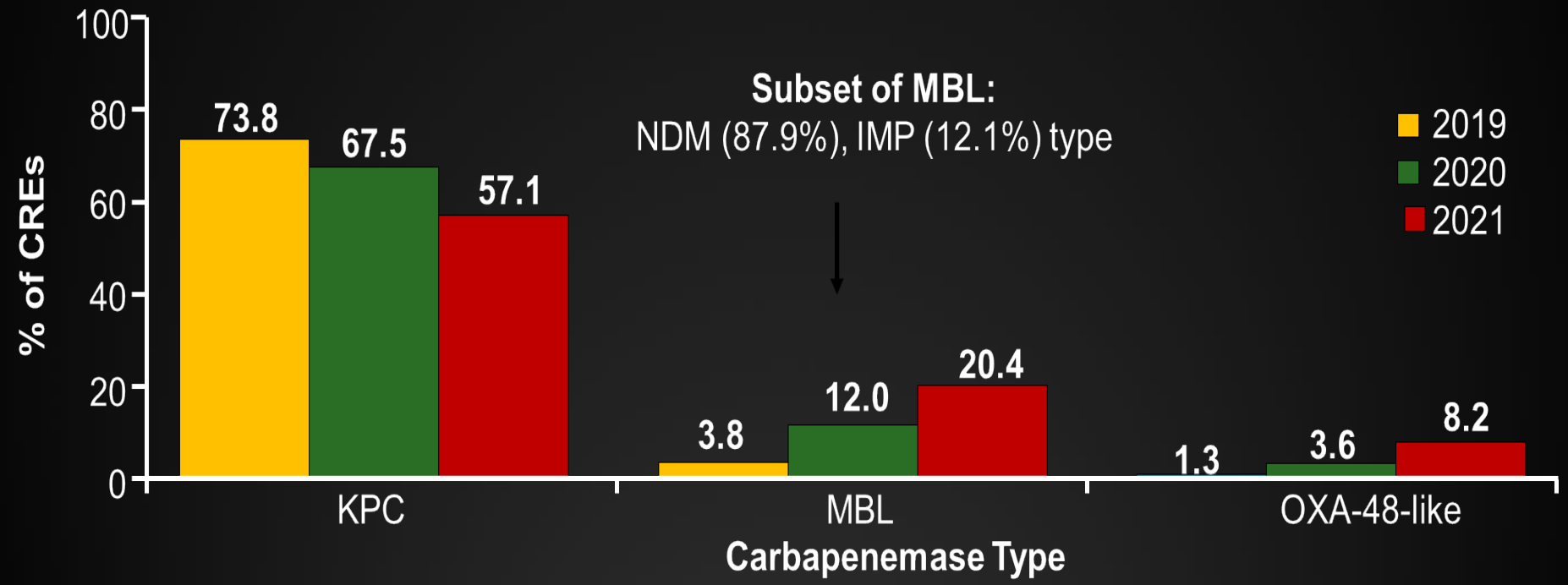
Place in therapy

5- Treatment of MDR pathogens

a) Gram positive
b) Gram negative

US Carbapenemases: Rise in NDM and OXA-48-like

Surveillance study of 27,834 *Enterobacterales* isolates from 74 US medical centers in 2019-2021



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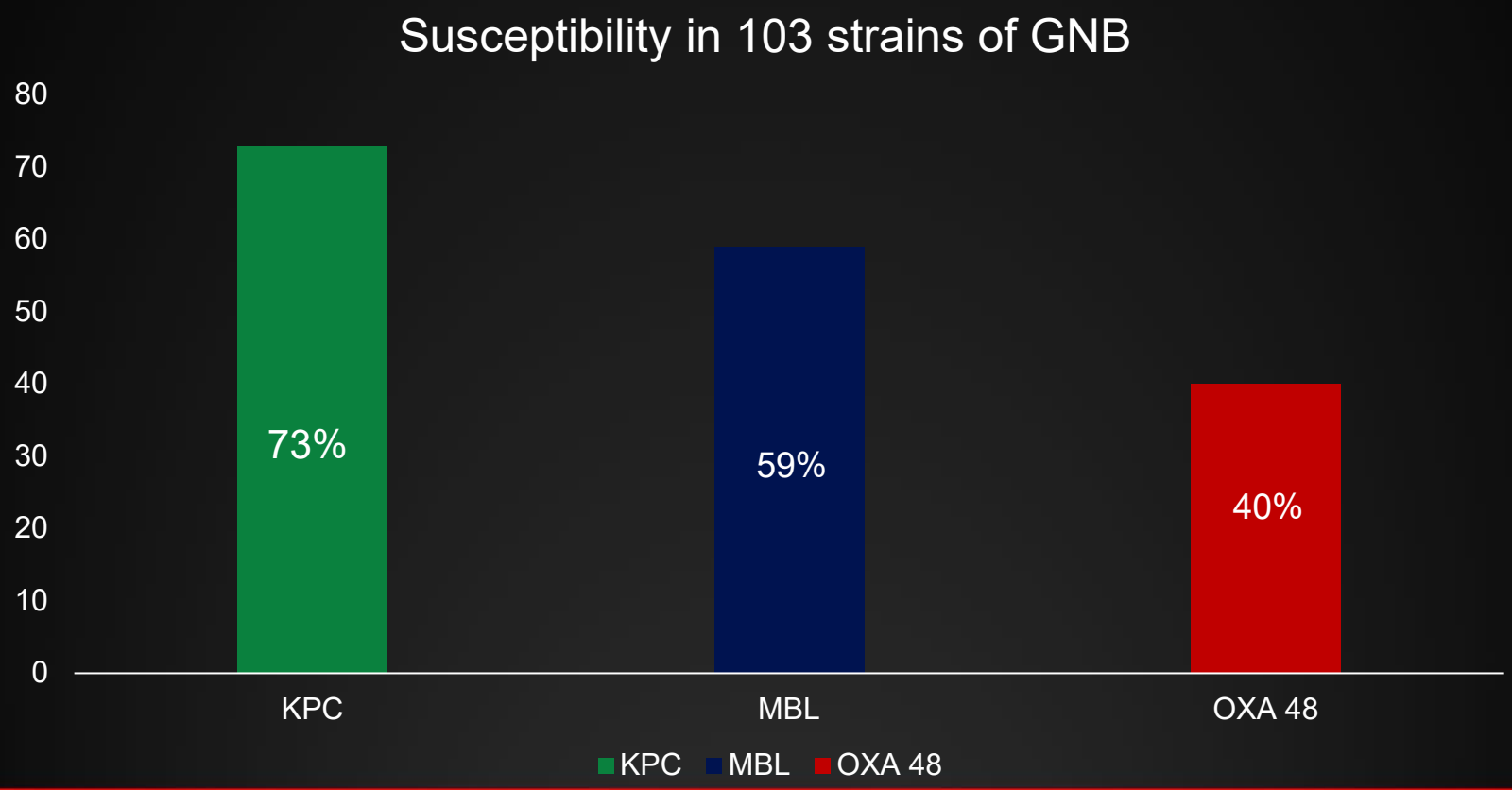
In Vitro Activity of Eravacycline against Carbapenemase-Producing Gram-Negative Bacilli Clinical Isolates in Central Poland



Brauncajs M. Biomedicine 2023

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Tetracycline Derivatives for CRE

- Activity not impacted by β-lactamase type
- **Tigecycline and eravacycline:** alternative options for intra-abdominal, skin and soft tissue, osteomyelitis, and respiratory CRE infections

Caution

- Avoid for BSI and UTI: blood and urine concentrations insufficient
  - ➢ Eravacycline failed in 2 phase III UTI trials
- No CLSI breakpoints for tigecycline or eravacycline

Tamma. Clin Infect Dis. 2024;ciae403. Tigecycline PI. Eravacycline PI.
Lauf. Diagn Microbiol Infect Dis. 2014;78:469. Solomkin. Clin Infect Dis. 2019;69:921

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Other CRAB infections

- 46 pts treated with ERV for *A. baumannii* (69.5% CRAB)
- Infections: lung 58.3%; COMBO in 84.4%.
- Median ERV 6.9 days (5.1 to 11.1).

TABLE 1 (Continued)

Parameter	Result for[b]: Population ($n = 46$)	CRAB ($n = 32$)
Intensive care upon index culture, *n* (%)[c]	19 (41.3)	14 (43.8)
SOFA score, median (IQR)	4.0 (2.0–7.0)	5.0 (2.3–7.0)
Mechanical ventilation, *n* (%)	18 (39.1)	14 (43.8)
For ≥ 48 h	18 (100)	14 (100)
Surgery consult, *n* (%)	17 (37.0)	13 (40.6)
Source control, *n* (%)[f]	20 (43.5)	16 (50)
Infectious Diseases consult, *n* (%)	45 (97.8)	31 (96.9)
Within 48 h[g]	34/45 (75.5)	25/31 (80.6)
Switched to another agent, *n* (%)	6 (13.0)	3 (9.4)
Minocycline	3 (6.5)	1 (3.1)
Other[e]	3 (6.5)	2 (6.2)
Clinical outcomes		
30-day mortality, *n* (%)	11 (23.9)	7 (21.9)
90-day mortality, *n* (%)	14 (30.4)	10 (31.3)
30-day recurrence, *n* (%)	10 (21.7)	8 (25.0)
Excluding patients with 30-day mortality	7 (20.0)	6 (24.0)
30-day readmission, *n* (%)	7 (15.2)	5 (15.6)
Excluding patients with 30-day mortality	6 (17.1)	4 (16.0)
Symptoms of infection worsen or fail to resolve, *n* (	13 (28.3)	9 (28.1)
Excluding patients with 30-day mortality	7 (20.0)	4 (16.0)
LOS, median (IQR)		
Total	21 (12.5–39.0)	22 (13.0–39.5)
Before index culture	13.6 (10.1–30.9)	14.3 (10.5–31.5)
ICU	23.0 (16.5–46.5)	23.5 (16.5–47.0)
ERV-possible adverse events, *n* (%)		
Gastrointestinal	1 (2.2)	1 (3.1)

Acinetobacter baumannii

24 COVID-19 pts with CRAB pneumonia treated with eravacycline combo tx

	N=24
LENGHT OF ERAV. Tx	10.5 d
CLINICAL RESOLUTION	17 (71%)
MICROBIOLOGICAL CURE	12/17 (71%)
ADVERSE EVENTS	0

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Place in therapy

6-Alternative to Beta-lactams and FQ

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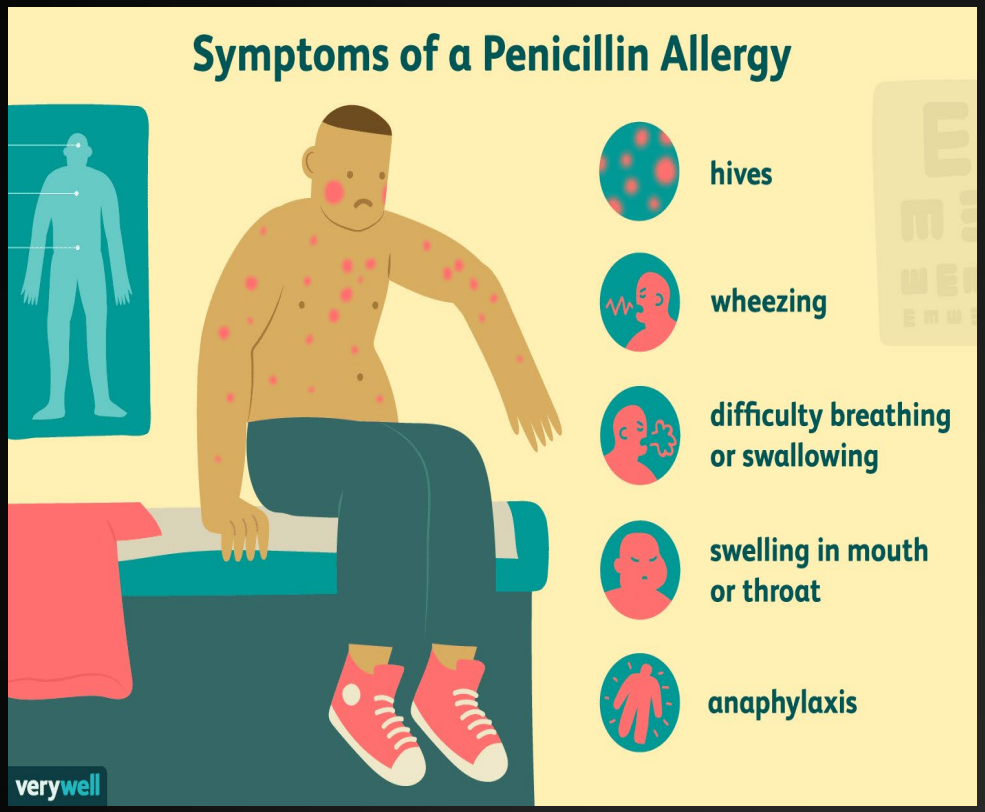
Eravacycline



Patients with penicillin allergy

Patients with intolerant or w AE

CARBA-sparing (IGNITE 1!)

Pts at high risk for C. diff infections?

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Place in therapy

7-Other infections

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Other opportunities…

1

In Vitro Activities of Eravacycline and Other Antimicrobial Agents against Human Mycoplasmas and Ureaplasmas

Waites. AAC 2020

2

In Vitro Susceptibility Testing of Eravacycline against Nontuberculous Mycobacteria

AAC 2022

Barbara A. Brown-Elliott,[a] Richard J. Wallace, Jr.[a]

3

In vitro activity of eravacycline against common ribotypes of *Clostridioides difficile*

JAC 2022

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Place in therapy

8-Economic considerations

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Costs

The launching wholesale acquisition cost of eravacycline is $44 per vial or **$702-$2464** for a 4 to 24-day course, which is at least 3 times less than the least expensive branded antimicrobial with similar spectrum

Conclusions

- Overall, ERV provides a novel therapeutic alternative for patients with cIAI.
- This antimicrobial is particularly valuable as empiric therapy when broad coverage (including MDR) is required, and for patients intolerant or allergic to b-lactam agents or fluoroquinolones.
- Real-world clinical experience with ERV, particularly beyond its use in cIAI, is warranted to adequately confirm its potential use in daily clinical practice.

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JAMA Surgery | Original Investigation

Assessing the Efficacy and Safety of Eravacycline vs Ertapenem in Complicated Intra-abdominal Infections in the Investigating Gram-Negative Infections Treated With Eravacycline (IGNITE 1) Trial

A Randomized Clinical Trial

Non inferiority trial
Randomized clinical trial (1:1)
Double-blind
Multicenter study
66 sites, 11 countries

Eravacycline, 1.0 mg/kg every 12 hours

Ertapenem 1.0 g every 24 hours

Solomkin J, Evans D, Slepavicius A, et al. JAMA Surg. 2017;152(3):224-232.

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A Randomized Clinical Trial

Primary endpoint: Clinical response at TOC in micro-ITT for FDA and in the MITT and CE populations for EMA

Eravacycline	Ertapenem
270 patients	271 patients
87.0%	**88.8%**
Clinical cure in the MITT	**Clinical cure in the MITT**

Solomkin J, Evans D, Slepavicius A, et al. JAMA Surg. 2017;152(3):224-232.

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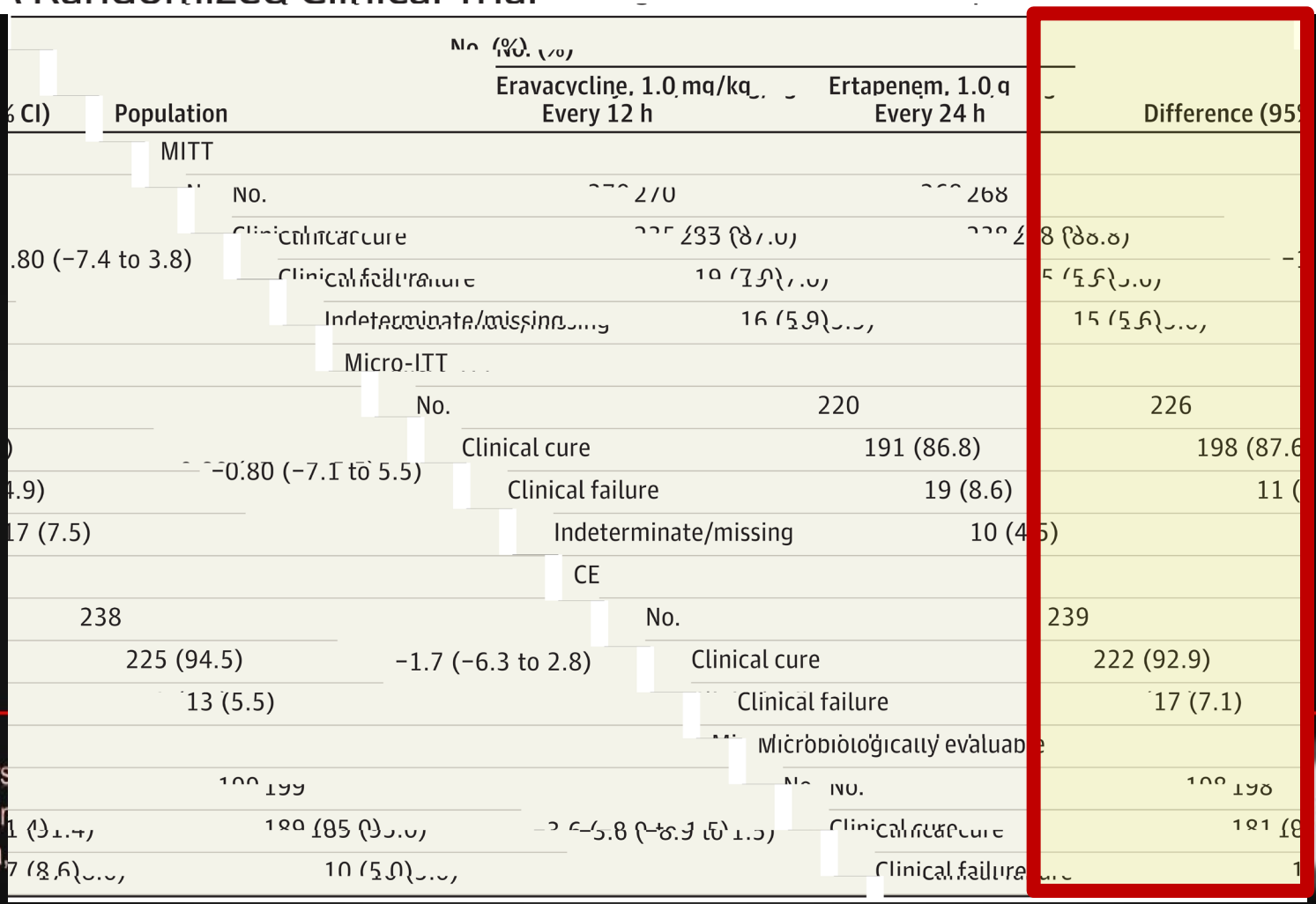

% CI)	Population	Eravacycline, 1.0 mg/kg, Every 12 h	Ertapenem, 1.0 g Every 24 h	Difference (95
	MITT			
	No.	270	268	
.80 (−7.4 to 3.8)	Clinical cure	233 (87.0)	238 (88.8)	
	Clinical failure	19 (7.0)	15 (5.6)	
	Indeterminate/missing	16 (5.9)	15 (5.6)	
	Micro-ITT			
	No.	220	226	
	Clinical cure	191 (86.8)	198 (87.6	
−0.80 (−7.1 to 5.5)	Clinical failure	19 (8.6)	11 (	
4.9)	Indeterminate/missing	10 (4.5)		
17 (7.5)	CE			
	No.	238	239	
	Clinical cure	225 (94.5)	222 (92.9)	
−1.7 (−6.3 to 2.8)	Clinical failure	13 (5.5)	17 (7.1)	
	Microbiologically evaluable			
	No.	199	198	
	Clinical cure	189 (95.0)	181 (9	
	Clinical failure	10 (5.0)	17	

IGNITE 4 TRIAL
Hospitalized patients with cIAI

Clinical Infectious Diseases

MAJOR ARTICLE

IGNITE4: Results of a Phase 3, Randomized, Multicenter, Prospective Trial of Eravacycline vs Meropenem in the Treatment of Complicated Intraabdominal Infections

Joseph S. Solomkin,[1] Janis Gardovskis,[2] Kenneth Lawrence,[3] Philippe Montravers,[4,5,6] Angie Sway,[7] David Evans,[8] and Larry Tsai[3]

[1]Department of Surgery, University of Cincinnati College of Medicine, Ohio; [2]Department of Surgery, Riga Stradins University, Latvia; [3]Tetraphase Pharmaceuticals, Watertown, Massachusetts; [4]Département d'Anesthésie-Réanimation, CHU Bichat Claude Bernard [5]Université Paris Diderot, PRESS Sorbonne Cité, and [6]Institut National de la Santé et de la Recherche Médicale (INSERM) UMR 1152, Paris, France; and [7]World Surgical Infection Society, Cincinnati, Ohio and [8]Department of Surgery, Ohio State University School of Medicine, Columbus

Primary endpoint: clinical cure rates at the test-of-cure visit (25-31 d from start of tx) in the microbiological intent-to-treat population

IGNITE 4 TRIAL
Hospitalized patients with cIAI

Population	Eravacycline	Meropenem	Difference (95% Confidence Interval)
Modified intent-to-treat	N = 250	N = 249	…
Clinical cure	231 (92.4)	228 (91.6)	0.8 (–4.1, 5.8)
Clinical failure	7 (2.8)	9 (3.6)	…
Indeterminate/Missing	12 (4.8)	12 (4.8)	…
Microbiological intent-to-treat	N = 195	N = 205	…
Clinical cure	177 (90.8)	187 (91.2)	–0.5 (–6.3, 5.3)
Clinical failure	7 (3.6)	7 (3.4)	…
Indeterminate/Missing	11 (5.6)	11 (5.4)	…
Clinically evaluable	N = 225	N = 231	…
Clinical cure	218 (96.9)	222 (96.1)	0.8 (–2.9, 4.5)
Clinical failure	7 (3.1)	9 (3.9)	…
Indeterminate/Missing	0	0	…
Microbiologically evaluable	N = 174	N = 194	…
Clinical cure	167 (96.0)	187 (96.4)	–0.4 (–4.9, 3.8)
Clinical failure	7 (4.0)	7 (3.6)	…
Indeterminate/Missing	0	0	…