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In vitro activity of eravacycline and comparator agents against bacterial pathogens isolated from patients with cancer

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Background: Bacterial infections are common in patients with cancer, and many bacteria have developed resistance to currently used antibiotics.

Objectives: We evaluated the *in vitro* activity of eravacycline (a recently developed fluorocycline) and comparators against bacterial pathogens isolated from patients with cancer.

Methods: Antimicrobial susceptibility testing was performed using CLSI-approved methodology and interpretive criteria for 255 Gram-positive and 310 Gram-negative bacteria. MIC and susceptibility percentage were calculated according to CLSI and FDA breakpoints when available.

Results: Eravacycline had potent activity against most Gram-positive bacteria, including MRSA. Of 80 Gram-positive isolates with available breakpoints, 74 (92.5%) were susceptible to eravacycline. Eravacycline had potent activity against most Enterobacterales, including ESBL-producing organisms. Of 230 Gram-negative isolates with available breakpoints, 201 (87.4%) were susceptible to eravacycline. Eravacycline had the best activity among comparators against carbapenem-resistant Enterobacterales, with 83% susceptibility. Eravacycline was also active against many non-fermenting Gram-negative bacteria, with the lowest MIC_{90} value among comparators.

Conclusions: Eravacycline was active against many clinically significant bacteria isolated from patients with cancer, including MRSA, carbapenem-resistant Enterobacterales, and non-fermenting Gram-negative bacilli. Eravacycline might play an important role in the treatment of bacterial infections in patients with cancer, and additional clinical evaluation is warranted.

Introduction

Cancer-associated bacterial infections are common, not only in patients with haematological malignancies, especially during episodes of neutropenia, but also in non-neutropenic patients with solid tumours.[1–3] For several decades, Gram-positive bacteria (GPB) have been the predominant bacterial pathogens in patients with cancer.[4] However, recent data have documented an epidemiological shift at many cancer treatment centres, with the re-emergence of Gram-negative bacteria (GNB) as frequent pathogens in this setting.[5,6] Currently, GNB and GPB are the documented cause of ∼40%–45% of bacterial infections at our institution (a National Cancer Institute-designated comprehensive cancer centre), whereas ∼10%–15% are polymicrobial.[5–7] Many of these pathogens (both GPB and GNB) have become problematic owing to the emergence of resistance to antimicrobial agents commonly used in this setting.[8] Consequently, newer agents with potential activity against clinically important bacterial species, including resistant strains, are urgently needed.

Unfortunately, during the preclinical and clinical evaluation of most novel agents, immunosuppressed patients, including those with cancer, are routinely excluded. Thus, *in vitro* and clinical data relating to this relatively high-risk population are limited or even non-existent. Eravacycline is a recently developed fluorocycline that is not susceptible to common mechanisms causing tetracycline resistance (e.g. efflux pumps, ribosomal protection

proteins).[9,10] Eravacycline has been shown to be active against GPB such as staphylococci, including MRSA, and enterococci, including VRE, as well as many GNB, including ESBL-producing organisms, and carbapenem-resistant Enterobacterales (CRE).[11–13] We believe that eravacycline might have a role to play in the treatment of some bacterial infections in patients with cancer, particularly in this era of emerging resistance. As a first step, we evaluated the *in vitro* activity of eravacycline and selected comparator agents against clinical isolates recovered exclusively from patients with cancer being treated at The University of Texas MD Anderson Cancer Center.

Materials and methods

We evaluated the *in vitro* activity of eravacycline and comparator agents commonly used in patients with cancer against 255 GPB and 310 GNB recently isolated (2018–20) from patients being treated at MD Anderson. These bacteria were exclusively blood culture isolates, processed in our institution's clinical microbiology laboratory and stored in our Institutional Review Board-approved research repository. Only one isolate per patient was tested (i.e. no duplicate isolates). Among GNB, 60 ESBL-producing and 30 CRE isolates were tested. ESBLs are defined as enzymes produced by certain bacteria that are able to hydrolyse extended-spectrum cephalosporins, based on data from our microbiology laboratory as generated by the VITEK 2 system. CRE analysis at our microbiology laboratory is based upon susceptibility data. Eravacycline powder was provided by the sponsor, Tetraphase Pharmaceuticals, and comparator agents were purchased from reliable commercial sources for *in vitro* testing. Comparator agents for GPB were daptomycin, linezolid and vancomycin. Comparator agents for GNB were amikacin, cefepime, ceftazidime/avibactam, ciprofloxacin, meropenem, piperacillin/tazobactam and tigecycline.

Susceptibility testing was performed using CLSI-approved broth microdilution methodology.[14,15] Appropriate ATCC control organisms (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Klebsiella pneumoniae* ATCC 700603 for GNB, and *Staphylococcus aureus* ATCC 29213 and *Enterococcus faecalis* ATCC 29212 for GPB) were included in each run to ensure the accuracy and validity of our results. Lysed horse blood (5% v/v) was used in broth microdilution susceptibility testing of streptococci. Mueller–Hinton broth supplemented with calcium for daptomycin testing was used, as recommended by CLSI. Fresh medium was used in every single run.

The *in vitro* activity of each agent was reported using MIC. The MIC_{50}, MIC_{90} and MIC range, as well as percentage susceptibility, were calculated according to CLSI methods.[14,15] The percentage susceptibility was determined using CLSI breakpoints. FDA breakpoints were used when no CLSI breakpoints were available.

P values were calculated using the Fisher exact test to identify significant ($P < 0.05$) differences in MIC between only eravacycline and ciprofloxacin for ESBL-positive *E. coli* and between eravacycline and ceftazidime/avibactam for CRE.

Results

The *in vitro* activity of eravacycline and three comparators against 255 GPB is depicted in Table 1. Overall, 74 of 80 GPB isolates (92.5%) with available FDA breakpoints were susceptible to eravacycline at ≤0.06 mg/L, and susceptibility rates to daptomycin, linezolid and vancomycin for the same isolates were 96.7%, 97.5% and 75%, respectively. The *in vitro* activity of eravacycline and comparator agents against 310 GNB is shown in Table 2.

Activity against staphylococci

All 40 *S. aureus* isolates (20 MRSA and 20 MSSA) were susceptible to eravacycline and comparators based on FDA breakpoint criteria. Although susceptibility breakpoints are not available, eravacycline inhibited all 20 oxacillin-susceptible CoNS at ≤0.06 mg/L. Three of 20 oxacillin-resistant CoNS isolates (15%) were inhibited by eravacycline, at an MIC of >0.06 mg/L for these isolates.

The susceptibility breakpoint for *Staphylococcus lugdunensis* is not currently established; however, eravacycline inhibited all 10 tested isolates at ≤0.06 mg/L, with the lowest MIC_{50} (≤0.015 mg/L) and MIC_{90} (≤0.03 mg/L) values among comparators.

Activity against enterococci

Eighty-five percent of vancomycin-susceptible *E. faecalis* and 85% of vancomycin-resistant *Enterococcus faecium* were susceptible to eravacycline. Three of 20 vancomycin-susceptible *E. faecalis* and three of 20 vancomycin-resistant *E. faecium* species had eravacycline MIC values >0.06 mg/L, and based on FDA breakpoint criteria, these isolates were not susceptible to eravacycline.

Activity against streptococci

All 30 *S. pneumoniae* isolates (15 penicillin susceptible and 15 penicillin resistant), all 18 isolates of β-haemolytic streptococci (4 *Streptococcus pyogenes*, 10 *Streptococcus agalactiae*, and 4 group G streptococci) and all 32 viridans group streptococci were inhibited by ≤0.06 mg/L eravacycline. All comparator agents with available breakpoints were also active against these isolates.

Susceptibility breakpoints for less common GPB are not currently established; however, eravacycline inhibited all tested isolates of *Bacillus*, *Corynebacterium* and *Micrococcus* species at ≤0.06 mg/L.

Activity against Enterobacterales

All 60 *E. coli* isolates (30 ESBL positive and 30 ESBL negative) were inhibited by ≤0.5 mg/L eravacycline with 100% susceptibilities. All 30 ESBL-positive *E. coli* species were susceptible to eravacycline but resistant to ciprofloxacin ($P < 0.001$). In addition, 80 of 90 (88.9%) *Klebsiella* species (30 *Klebsiella oxytoca* and 60 *K. pneumoniae*, both ESBL positive and ESBL negative) were susceptible to eravacycline. All 10 *Citrobacter* species isolates were susceptible to eravacycline. *Enterobacter cloacae* had 83% susceptibility to eravacycline, with MIC_{50} and MIC_{90} values of 0.25 and 2 mg/L respectively. Also, eravacycline inhibited 25 of 30 (83%) CRE pathogens (12 *K. pneumoniae*, 10 *E. coli* and 8 *E. cloacae*) at ≤0.5 mg/L, with the lowest MIC_{50} (0.25 mg/L) and MIC_{90} (1 mg/L) among the comparators. In contrast, only 53% of CRE isolates were susceptible to ceftazidime/avibactam ($P = 0.025$). The susceptibility of CRE to other comparators varied from 17% with cefepime and ciprofloxacin to 73% with tigecycline. The MIC_{90} values of eravacycline were 4-fold lower than that of tigecycline against CRE isolates, 2-fold lower than that of tigecycline against ESBL-positive *E. coli*, and 8-fold lower than that of tigecycline against ESBL-positive *K. pneumoniae* isolates.

Table 1. *In vitro* activity of eravacycline and three comparators against 255 GPB isolated from patients with cancer[a]

Organism	No. tested	Agent	% S[b]	MIC (mg/L)		
				MIC_{50}	MIC_{90}	Range
Bacillus species	15	Eravacycline	NA	≤0.015	0.03	≤0.015–0.03
		Daptomycin	NA	1	4	≤0.25–4
		Linezolid	NA	1	4	0.5–16
		Vancomycin	NA	0.5	1	0.06–1
β-Haemolytic streptococci	18	Eravacycline	NA	≤0.015	0.03	≤0.015–0.06
		Daptomycin	100	≤0.25	0.5	≤0.25–1
		Linezolid	100	1	2	≤0.25–2
		Vancomycin	100	0.125	0.5	0.06–0.5
Corynebacterium species	15	Eravacycline	NA	≤0.015	0.06	≤0.015–0.06
		Daptomycin	NA	≤0.25	0.5	≤0.25–0.5
		Linezolid	NA	≤0.25	0.5	≤0.25–1
		Vancomycin	NA	0.25	0.5	0.06–0.5
Vancomycin-susceptible *E. faecalis*	20	Eravacycline	85	0.06	0.125	0.03–1
		Daptomycin	90	2	2	0.5–4
		Linezolid	95	1	2	0.5–4
		Vancomycin	100	0	2	0.5–2
Vancomycin-resistant *E. faecium*	20	Eravacycline	85	0.06	0.25	0.03–0.5
		Daptomycin	NA	2	4	1–8
		Linezolid	95	1	2	1–8
		Vancomycin	0	>128	>128	>128
Micrococcus species	15	Eravacycline	NA	0.06	0.06	≤0.015–0.06
		Daptomycin	NA	≤0.25	0.5	≤0.25–16
		Linezolid	NA	0.5	0.5	≤0.25–1
		Vancomycin	NA	0.125	0.25	0.06–2
MRSA	20	Eravacycline	100	≤0.015	≤0.015	≤0.015–0.06
		Daptomycin	100	≤0.25	0.5	≤0.25–1
		Linezolid	100	1	2	1–2
		Vancomycin	100	1	1	0.5–1
MSSA	20	Eravacycline	100	≤0.015	≤0.015	≤0.015–0.06
		Daptomycin	100	≤0.25	≤0.25	≤0.25–0.5
		Linezolid	100	1	2	1–2
		Vancomycin	100	1	1	0.5–1
CoNS (oxacillin resistant)	20	Eravacycline	NA	0.06	0.125	0.03–0.25
		Daptomycin	100	0.5	1	≤0.25–1
		Linezolid	75	0.5	8	≤0.25 to >32
		Vancomycin	100	0.25	0.5	0.25–0.5
CoNS (oxacillin susceptible)	20	Eravacycline	NA	0.06	0.06	≤0.015–0.25
		Daptomycin	100	0.5	1	≤0.25–1
		Linezolid	95	0.5	1	≤0.25 to >32
		Vancomycin	100	1	1	0.25–2
S. lugdunensis	10	Eravacycline	NA	≤0.015	0.03	≤0.015–0.06
		Daptomycin	100	≤0.25	0.5	≤0.25–0.5
		Linezolid	100	0.5	0.5	0.5–1
		Vancomycin	100	0.5	0.5	0.25–0.5
S. pneumoniae (15 penicillin susceptible and 15 penicillin resistant)	30	Eravacycline	NA	0.03	0.06	≤0.015–0.06
		Daptomycin	NA	≤0.25	≤0.25	≤0.25–0.5
		Linezolid	100	0.5	0.5	≤0.25–1
		Vancomycin	100	0.06	0.06	≤0.03–0.125

Continued

Table 1. *Continued*

Organism	No. tested	Agent	% S[b]	MIC (mg/L)		
				MIC_{50}	MIC_{90}	Range
Viridans group streptococci	32	Eravacycline	NA	≤0.015	0.06	≤0.015–0.06
		Daptomycin	97	≤0.25	1	≤0.25–2
		Linezolid	100	≤0.25	1	≤0.25–2
		Vancomycin	100	0.125	0.5	≤0.03–1

[a]% S, percentage of susceptibility; NA, not applicable, either because breakpoints have not been established for the antimicrobial agent/bacterial species combination or because the antimicrobial agent is not expected to have activity against the bacterial species.
[b]FDA susceptibility breakpoint for eravacycline against *S. aureus* (MRSA and MSSA), *E. faecalis* (vancomycin susceptible) and *E. faecium* (vancomycin resistant) is ≤0.06 mg/L.

Activity against non-fermenting GNB

Although susceptibility breakpoints for non-fermenting GNB are not currently established, the MIC_{90} values of eravacycline were the lowest among other comparators: 1 mg/L for *Achromobacter* species, 1 mg/L for *Acinetobacter* species, 0.25 mg/L for *Sphingomonas paucimobilis* and 2 mg/L for *Stenotrophomonas maltophilia*. Altogether, 56 of 80 of these isolates (70%) were inhibited by ≤0.5 mg/L eravacycline. The MIC_{90} values of eravacycline were 2-fold to 4-fold lower than that of tigecycline against most of the non-fermenting GNB isolates (such as *Achromobacter* and *S. maltophilia*).

Discussion

Eravacycline has been approved by the FDA for the treatment of complicated intra-abdominal infections caused by susceptible organisms in patients aged 18 years or older.[16] Immunosuppressed patients, such as patients with cancer, are routinely excluded during the evaluation of novel antimicrobial agents, including eravacycline, leading to a paucity of preclinical and clinical data on the efficacy of eravacycline in this patient population.

To the best of our knowledge, the current study is the first to focus on bacterial pathogens isolated from patients with cancer. Our data on the *in vitro* activity of eravacycline against bacterial isolates recovered from patients with cancer are similar to those generated from other patient populations and confirm that eravacycline is active against most GPB and GNB, including MDR organisms such as MRSA, VRE, CRE and ESBL-producing organisms,[17–20] with the notable exclusion of *P. aeruginosa*, which was not tested in our study. This gap in coverage makes eravacycline unsuitable for empirical monotherapy in high-risk cancer patients hospitalized with fever and neutropenia, in whom *P. aeruginosa* is a frequent cause of infection. However, eravacycline could be used in combination with an antipseudomonal agent (cephalosporin or carbapenem) in these patients, particularly those who are known to be colonized with resistant GNB other than *P. aeruginosa*.

Over the past two decades, the wide empirical use of β-lactams and the prolonged prophylactic use of quinolones in neutropenic cancer patients has resulted in escalating rates of emerging resistant GNB such as CRE and ESBL-producing organisms, in addition to resistant GPB such as MRSA and VRE.[21,22] Hence, empirical monotherapy with antipseudomonal β-lactams in high-risk febrile neutropenic cancer patients fails to cover most of these resistant organisms. Based on our data and that of other investigators, the addition of eravacycline to an antipseudomonal β-lactam in this high-risk febrile neutropenic patient population would be most appropriate. The fact that eravacycline was significantly more active against CRE organisms than was ceftazidime/avibactam and the fact that all ESBL-positive *E. coli* were susceptible to eravacycline and resistant to ciprofloxacin supports our proposition of using eravacycline in combination with antipseudomonal β-lactams for the treatment of high-risk patients with neutropenic febrile cancer. Two large prospective multicentre randomized trials (IGNITE 1 and IGNITE 2) have shown that eravacycline efficacy and safety in treating complicated intra-abdominal infections and associated secondary bacteraemia are similar to that of meropenem and ertapenem.[23–25] This has important implications for non-neutropenic patients with intra-abdominal tumours that result in altered intra-abdominal anatomy (such as obstruction, perforation or fistula), resulting in complicated intra-abdominal infections. Eravacycline activity against the highly resistant enteric organisms such as VRE and CRE would make it a useful agent in this patient population.

Our data are in agreement with other *in vitro* studies in showing that eravacycline potency is 2-fold to 4-fold greater than that of tigecycline against most of the tested Enterobacterales, particularly resistant GNB such as CRE and ESBL-producing organisms, as well as non-fermenting GNB as *S. maltophilia*.[17] This, in addition to the better tolerability profile for eravacycline compared with tigecycline, could make eravacycline a potential alternative agent (alone or in combination) in patients with these specific infections.[23,24,26] However, some researchers reported that four patients with *Acinetobacter baumannii* bacteraemia died while receiving an eravacycline-based antibiotic regimen. Therefore, eravacycline may carry poor outcomes in bacteraemia, if bacteraemia is in the setting of pneumonia, conversely to bacteraemia in the setting of complicated intraabdominal infection (IGNITE 1).[27]

Other potential indications for eravacycline use in patients with cancer include targeted therapy against isolated pathogens that are susceptible to it, and step-down therapy to facilitate hospital discharge in neutropenic patients without pseudomonal

Table 2. *In vitro* activity of eravacycline and seven comparators against 310 Gram-negative bacteria isolated from patients with cancer[a]

Organism	No. tested	Agent[b]	% S[c]	MIC (mg/L)		
				MIC_{50}	MIC_{90}	Range
Achromobacter species	15	Eravacycline	NA	0.5	1	0.03–1
		Amikacin	NA	64	256	2 to >256
		Cefepime	NA	64	>128	16 to >128
		CZA	NA	4	16	0.5–16
		Ciprofloxacin	NA	4	>32	1 to >32
		Meropenem	NA	0.5	16	0.06–32
		TZP	NA	1	64	≤0.5–64
		Tigecycline	NA	2	2	0.25–4
Acinetobacter species	20	Eravacycline	NA	0.125	1	0.03 to >2
		Amikacin	100	1	4	0.5–4
		Cefepime	70	2	128	0.25 to >128
		CZA	NA	8	64	2 to >128
		Ciprofloxacin	85	0.25	2	0.06–32
		Meropenem	70	0.25	>32	0.06 to >32
		TZP	60	4	128	≤0.5 to >512
		Tigecycline	NA	0.25	1	≤0.06–4
Citrobacter species	10	Eravacycline	100	0.125	0.5	0.06–0.5
		Amikacin	100	1	2	0.5–2
		Cefepime	70	0.5	8	0.125–16
		CZA	100	0.5	2	0.25–8
		Ciprofloxacin	0	1	4	1–8
		Meropenem	70	≤0.03	0.6	≤0.03–0.125
		TZP	20	128	>512	8 to >512
		Tigecycline	100	1	2	0.5–2
CRE	30	Eravacycline	83	0.25	1	0.0015 to >2
(10 *E. coli*, 12 *K. pneumoniae*, 8 *E. cloacae*)		Amikacin	60	8	>256	≤0.05 to >256
		Cefepime	17	>128	>128	0.5 to >128
		CZA	53	4	>128	0.125 to >128
		Ciprofloxacin	17	8	>32	≤0.015 to >32
		Meropenem	3	8	>32	2.0 to >32
		TZP	13	>512	>512	8 to >512
		Tigecycline	73	1	4	0.125–8
E. cloacae	30	Eravacycline	83	0.25	2	0.0075 to >2
		Amikacin	100	1	2	≤0.25–4
		Cefepime	90	≤0.125	4	≤0.125–128
		CZA	100	0.25	1	≤0.125–4
		Ciprofloxacin	87	≤0.03	1	≤0.03–16
		Meropenem	97	≤0.03	0.125	≤0.03–16
		TZP	73	8	256	1 to >512
		Tigecycline	90	0.5	2	0.125–8
E. coli (ESBL positive)	30	Eravacycline	100	0.25	0.5	0.06–0.5
		Amikacin	100	4	8	0.5–8
		Cefepime	23	16	>128	≤0.125 to >128
		CZA	90	0.5	8	≤0.125 to >128
		Ciprofloxacin	0	>32	8	0.5–8
		Meropenem	100	0.25	0.5	≤0.03–0.5
		TZP	60	16	512	2 to >512
		Tigecycline	100	1	1	0.5–2
E. coli	30	Eravacycline	100	0.015	0.25	0.0037–0.5
(ESBL negative)		Amikacin	100	2	2	0.5–32
		Cefepime	70	≤0.125	16	≤0.125 to >128

Continued

Table 2. *Continued*

Organism	No. tested	Agent[b]	% S[c]	MIC (mg/L)		
				MIC_{50}	MIC_{90}	Range
		CZA	100	≤0.125	0.25	≤0.125–2
		Ciprofloxacin	27	2	>32	≤0.03 to >32
		Meropenem	100	≤0.03	≤0.03	≤0.03–16
		TZP	77	4	128	1 to >512
		Tigecycline	100	0.25	0.5	≤0.06–2
K. oxytoca	30	Eravacycline	90	0.25	0.5	0.015–2
		Amikacin	93	1	8	≤0.25 to >256
		Cefepime	80	≤0.125	8	≤0.125–64
		CZA	97	≤0.125	1	≤0.125–16
		Ciprofloxacin	73	≤0.03	16	≤0.03 to >32
		Meropenem	90	≤0.03	0.125	≤0.03 to >32
		TZP	70	4	>512	1.0 to >512
		Tigecycline	97	1	2	0.5–4
K. pneumoniae (ESBL negative)	30	Eravacycline	93	0.25	0.5	0.06–1
		Amikacin	100	1	1	≤0.25–1
		Cefepime	100	<0.125	0.25	≤0.125–1
		CZA	100	<0.125	1	≤0.125–2
		Ciprofloxacin	80	0.06	0.5	≤0.03–16
		Meropenem	100	≤0.03	≤0.03	≤0.03–0.25
		TZP	100	4	16	1–16
		Tigecycline	93	1	1	0.5–4
K. pneumoniae (ESBL positive)	30	Eravacycline	83	0.5	1	0.25 to >2
		Amikacin	100	2	8	0.5–8
		Cefepime	17	64	>128	0.5 to >128
		CZA	67	1	>128	≤0.125 to >128
		Ciprofloxacin	13	16	>32	≤0.03 to >32
		Meropenem	93	0.06	2	≤0.03–2
		TZP	NA	512	>512	4 to >512
		Tigecycline	73	2	8	0.5–8
Serratia species	10	Eravacycline	20	1	1	0.5–1
		Amikacin	100	2	2	1–2
		Cefepime	100	≤0.125	0.25	≤0.125–0.5
		CZA	100	0.25	0.5	≤0.125–0.5
		Ciprofloxacin	100	0.06	0.125	≤0.03–0.25
		Meropenem	100	≤0.03	0.06	≤0.03–0.06
		TZP	100	2	16	2–16
		Tigecycline	100	1	2	1–2
S. paucimobilis	10	Eravacycline	NA	0.125	0.25	0.0075–0.25
		Amikacin	NA	0.5	1	≤0.25–64
		Cefepime	NA	0.5	2	0.25–4
		CZA	NA	0.25	4	≤0.125 to >128
		Ciprofloxacin	NA	0.5	1	≤0.03–2
		Meropenem	NA	≤0.03	4	≤0.03–4
		TZP	NA	8	>512	4 to >512
		Tigecycline	NA	0.25	1	0.125–1

Continued

Table 2. *Continued*

Organism	No. tested	Agent[b]	% S[c]	MIC (mg/L)		
				MIC_{50}	MIC_{90}	Range
S. maltophilia	35	Eravacycline	NA	0.5	2	0.125–2
		Amikacin	NA	128	>256	8 to >256
		Cefepime	NA	64	128	16–128
		CZA	NA	64	128	1 to >128
		Ciprofloxacin	NA	2	16	0.5–32
		Meropenem	NA	>32	>32	32 to >32
		TZP	NA	>512	>512	128 to >512
		Tigecycline	NA	2	8	0.125–16

[a]% S, percentage of susceptibility; CZA, ceftazidime/avibactam; TZP, piperacillin/tazobactam; ESBL, ESBL-producing organisms; NA, not applicable, either because breakpoints have not been established for the antimicrobial agent/bacterial species combination or because the antimicrobial agent is not expected to have activity against the bacterial species.
[b]Avibactam and tazobactam were used at a concentration of 4 mg/L.
[c]The US FDA susceptibility breakpoint for eravacycline against Enterobacterales isolates is ≤0.5 mg/L.

infections whose condition has been stabilized in the hospital. The long half-life and pharmacokinetics of eravacycline could favour its use once per day on an outpatient basis, particularly as a step-down therapy.[26,28] Eravacycline might also be a useful agent for outpatient treatment in low-risk febrile neutropenic patients, in whom pseudomonal infections are exceedingly rare.[5–7]

In summary, our data suggest that eravacycline could have a role in several important clinical scenarios for patients with cancer and should be clinically evaluated for these indications. These scenarios include eravacycline use in combination with an anti-pseudomonal β-lactam as empirical therapy in high-risk neutropenic febrile cancer patients. In addition, eravacycline could be used as monotherapy or in combination with other agents in the treatment of intra-abdominal infections in non-neutropenic patients with cancer. Furthermore, eravacycline should be considered as a step-down therapy for resistant infections in neutropenic patients with cancer and as an empirical outpatient therapy for low-risk febrile neutropenic patients. However, until further studies have been conducted, clinicians should be cautious with the use of eravacycline monotherapy in the setting of bacteraemia.

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Transparency declarations

I. Raad, University of Texas MD Anderson Cancer Center, is the inventor of the nitroglycerin-based catheter lock solution technology licensed by Novel Anti-Infective Technologies, LLC, in which he and the University of Texas MD Anderson Cancer Center are shareholders. All others have no conflicts to disclose.

Author contributions

Conceptualization and design: K.R., B.G., R.P., I.R.; budget preparation and originating the project: K.R., R.P., I.R.; project administration: K.R., R.P., I.R.; laboratory methodology and support: B.G., I.R.; writing original draft: B.G.; writing, review and editing: K.R., B.G., N.L., S.A.S., R.P., I.R.; supervision: K.R., I.R.. All authors reviewed and finalized the manuscript.

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