Table 2. Dalbavancin Use Characteristics

Table 2. Dalbavancin Use Characteristics

	n (%)
Dosing Regimens Utilized	
1500 mg x 1	29 (55)
1500 mg x 2	13 (25)
1500 mg x1, followed by 1000 mg x1	1 (2)
1000 mg x 1	3 (6)
1000 mg weekly	1 (2)
1000 mg x1, followed by 500 mg weekly	3 (6)
1000 mg x1, followed by 375 mg weekly	1 (2)
760 mg x 1, followed by 375 mg x1	1 (2)
Reason for Selection: ***Dalbavancin was selected for one or more of the below reasons, all reasons given in medical record were noted so the denominator is > 52***	
History of IV drug use	25
Lack of safe home environment in which to receive daily IV antibiotics	11
Prior non-adherence to outpatient antibiotics	11
Clinical contraindications to alternative antibiotics	7
Adverse reaction to initial outpatient antibiotic	5
Lack of alternative outpatient options due to funding or insurance issues	5
Substance use, not IV drug use	3
Inability of patient to physically manage PICC	2
Patient refused PICC or daily outpatient IV antibiotics	2
Prior history of contaminated/manipulated PICC	2
Discharging to a setting that could not accommodate daily IV antibiotics	2
Prior treatment failure	1
Unclear	1
Treatment Setting	**Number of doses infused**
Inpatient	31
Outpatient Infusion Center	30
Home Infusion	16
Emergency Department	2

Footnote: IV = intravenous / PICC = peripherally inserted central catheter

Table 3. Clinical Endpoints

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	n (%)
Loss to follow-up by day 90	8 (15)
Readmission for any reason by day 30	13 (25)
Readmission for any reason between days 30-90	1 (2)
Readmission due to adverse effects	0
Recurrence or relapse of infection by day 30	11 (21)
Recurrence or relapse of infection between days 30-90	5 (10)
30-day mortality	0
90-day mortality	0

Conclusion. While our results suggest dalbavancin is well tolerated, questions about relapse rates in the treatment of complicated S. aureus infections remain. Further research is needed to evaluate clinical outcomes for dalbavancin compared to standard of care antibiotics and to better elucidate whether relapses were related to true antibiotic failure versus other complexities of the S. aureus infections.

Disclosures. **All Authors**: No reported disclosures

1269. Differences in Interpretative Breakpoints Between CLSI, FDA and EUCAST Impact Reporting of Susceptibility and Resistance to Cefiderocol

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Session: P-58. Novel Agents

Background. Cefiderocol (CFDC) is a siderophore cephalosporin with broad coverage of aerobic Gram-negative (GN) bacteria. Provisional breakpoints (BP) were approved by CLSI in 2018, with FDA and EUCAST providing clinical BP in 2019 and 2020, respectively; however, BPs differ markedly between organizations, reflecting differences in labelling, PK/PD standards and availability of clinical study data during regulatory review. Here we compare susceptibility rates based on these different BPs.

Methods. Susceptibility rates for each bacterial species were determined using CFDC BP from each organization and the MICs of 28,629 GN clinical isolates from 3 consecutive years of SIDERO-WT surveillance studies (2014–17). The analysis used all isolates and sub-grouped isolates based on meropenem (MEM) susceptibility (CLSI BP) or carbapenemase production.

Results. Within the overall Enterobacterales group, ≥98.5% isolates were interpreted as susceptible to CFDC regardless of BP used. However, the proportion of susceptible differed significantly (82.5–98.6%) when applied to MEM-non-susceptible (NS) isolates. Similarly, against most carbapenemase producers, susceptibility ranged from 80 to 100%, however for NDM producers, only 51% of isolates were defined as susceptible by FDA or EUCAST BP vs 84% using the CLSI BP. Against *Pseudomonas aeruginosa* including MEM-NS isolates, susceptibility was ≥94% despite different BPs recommended by FDA (1 mg/L), EUCAST (2 mg/L) and CLSI (4 mg/L). This changed the proportion of IMP-producing isolates classified as susceptible from 100% (CLSI) and 81% (EUCAST) to only 19% (FDA). Against other non-fermenters, susceptibility was ≥91% irrespective of BP used.

Table 1. Susceptibility rates against Enterobacterales based on breakpoints from each organization

Table 1. Susceptibility rates against Enterobacterales based on breakpoints from each organization

	Number of isolates	Rate (%)							
		FDA			CLSI			EUCAST	
		S (2)	I (4)	R (8)	S (4)	I (8)	R(16)	S (2)	R (4)
Enterobacterales	19,119	98.5	1.4	0.1	99.9	0.1	0.02	98.5	1.5
MEM-NS	640	82.5	16.1	1.4	98.6	1.4	0	82.5	17.5
KPC producer	235	83.0	17.0	0	100	0	0	83.0	17.0
NDM producer	45	51.1	33.3	15.6	84.4	15.6	0	51.1	48.9
OXA-48 producer	181	80.7	18.2	1.1	98.9	1.1	0	80.7	19.3
VIM producer	75	89.3	10.7	0	100	0	0	89.3	10.7

Table 2. Susceptibility rates against non-fermenters based on breakpoints from each organization

Table 2. Susceptibility rates against non-fermenters based on breakpoints from each organization

	Number of isolates	Rate (%)							
		FDA			CLSI			EUCAST	
		S (1)	I (2)	R (4)	S (4)	I (8)	R(16)	S (2)	R (4)
P. aeruginosa	4,942	97.7	1.7	0.6	99.96	0.04	0	99.4	0.6
MEM-NS	1,154	94.5	4.0	1.5	99.9	0.1	0	98.5	1.5
VIM producer	135	92.6	6.7	0.7	100	0	0	99.3	0.7
IMP producer	16	18.8	62.5	18.8	100	0	0	81.2	18.8
A. baumannii complex	3,231	-*	-	-	96.0	1.5	2.5	94.0**	6.0**
MEM-NS	1,899	-	-	-	94.9	2.3	2.8	91.8**	8.2**
B. cepacia complex	164	-	-	-	-	-	-	95.7**	4.3**
MEM-NS	53	-	-	-	-	-	-	90.6**	9.4**
S. maltophilia	1,173	-	-	-	99.8	0	0.2	99.7**	0.3**

*: not calculated due to no available breakpoint; **: PK-PD (non-species-related) breakpoints were applied

Conclusion. Differences in BPs between FDA, CLSI and EUCAST could impact on the reporting of susceptibility or resistance to CFDC, particularly for MEM-NS isolates. PK/PD model simulations support 100% fT >MIC up to an MIC of 4 mg/L, and in Phase 3 trials the mean trough concentration of unbound cefiderocol was >4 mg/L. The potential impact of these differences on clinical decision making are important as the greatest clinical utility for CDFC is expected to be in patients with carbapenem-resistant GN infections due to limited treatment options.

Disclosures. Yoshinori Yamano, PhD, Shionogi & Co., Ltd. (Employee) Miki Takemura, MSc, Shionogi & Co., Ltd. (Employee) Christopher Longshaw, PhD, Shionogi B.V. (Employee) Roger Echols, MD, Shionogi Inc. (Consultant)

1270. Early Real-world Evidence in the Use of Eravacycline for the Management of Draconian Infections

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Session: P-58. Novel Agents

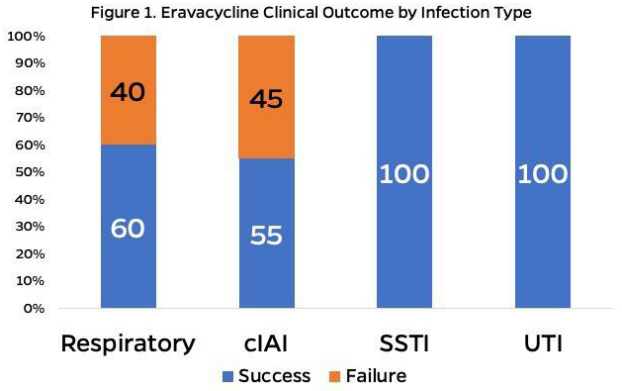
Background. Eravacycline (ERV) is a next-generation tetracycline approved for complicated intra-abdominal infections (cIAI) with *in-vitro* activity to multidrug-resistant organisms such as carbapenem resistant Enterobacteriaceae, extended spectrum beta-lactamase, and carbapenem-resistant *Acinetobacter baumannii* (CRAB). The purpose of this study was to identify the utility of ERV in clinical practice.

Methods. Retrospective case series was conducted on patients at AdventHealth that received at least two doses of ERV. Primary endpoint for the study was clinical success while on ERV, meeting none of the following criteria: changing therapy, mortality, or lack of improvement from sign/symptoms.

Results. Of 23 patients, 74% were males with a mean age of 55 ±18 years and mean body weight of 79 ±27 kg. Mean APACHE II and Charleson scores were 20 (±11) and 6 (±4), respectively. 91% received ERV for an off-label indication or organism. Infection types were respiratory (44%), cIAI (35%), skin (9%), and other (13%). All patients had positive cultures, while 61% were treated as a polymicrobial infection and 17% had bacteremia. Microorganisms included *A. xylosoxidans*, *S. maltophilia,* CRAB, and *K pneumoniae.* 48% had ERV susceptibilities from .06-4 mcg/mL, including two MIC ≥32mcg/mL for *S. maltophilia*. 70% were given another antibiotic prior to ERV with a median duration of 5 (1-35) days. Median duration of ERV was 8 (3-30) days. 83% percent received ERV in combination with another

antibiotic. During treatment, 26% had a Child-Pugh Class C at baseline and 30% had elevated liver function tests. No adverse drug reactions were reported. Upon discharge, 35% continued ERV. Clinical success was observed in 57% (12/21) of patients. Clinical outcome by infection type is summarized in Figure 1. Of 9 cases of clinical failure, 14% were changed to alternative, 19% died while on ERV, and 10% failed to resolve signs/symptoms. Two cases of *M. abscessus* infections had insufficient follow-up to assess clinical outcome.

Figure 1. Eravacycline Clinical Outcome by Infection Type



Conclusion. Initial real-world experience with ERV differs significantly from the trials regarding severity of illness, types of infection, and clinical outcomes. Further evaluation is necessary for using ERV as combination therapy and in off-label indications.

Disclosures. **All Authors**: No reported disclosures

1271. Efficacy and Safety of Cefiderocol and Best Available Therapy in Patients with Serious Infections Caused by Carbapenem-Resistant Gram-Negative Infections: Results of the Pathogen-Focused Phase 3 CREDIBLE-CR Study

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Session: P-58. Novel Agents

Background. The CREDIBLE-CR study assessed the efficacy and safety of cefiderocol (CFDC), a novel siderophore cephalosporin, in the treatment of serious infections due to carbapenem-resistant (CR) Gram-negative (GN) bacteria.

Methods. CREDIBLE-CR was an open-label, prospective, randomized 2:1, Phase 3 study (NCT02714595) in patients with nosocomial pneumonia (NP), bloodstream infections/sepsis (BSI/Sepsis), or complicated urinary tract infections (cUTI) with evidence of CR GN pathogens. Adults received intravenous CFDC 2 g, q8h, 3-h infusion or best available therapy (BAT; up to 3 drugs) for 7–14 days (extendable to 21 days). The primary endpoint at test of cure in the CR microbiological intent-to-treat (CR-MITT) population was clinical cure (NP, BSI/Sepsis) or microbiological eradication (cUTI). Secondary endpoints were clinical and microbiological outcomes, all-cause mortality (ACM) and safety. Only descriptive statistics were pre-specified.

Results. A total of 101 patients received CFDC and 49 received BAT (CR-MITT: CFDC n=80, BAT n=38): 50% had pneumonia, 31.4% BSI/Sepsis, and 18.6% cUTI (Table 1). Most frequent CR pathogens were *Acinetobacter baumannii* (45.8%), *Klebsiella pneumoniae* (37.3%), and *Pseudomonas aeruginosa* (23.7%). CFDC monotherapy was given to 83% of patients, while BAT monotherapy to 29% of patients. Primary outcome in the CFDC and BAT arms was achieved in 50.0% and 52.6% in NP, 43.5% and 42.9% in BSI/Sepsis, and 52.9% and 20.0% in cUTI patients (Figure). CFDC was highly efficacious vs CREs and NDM-producing pathogens. Day 28 ACM was 24.8% (25/101) with CFDC and 18.4% (9/49) with BAT. Rescue therapy was given more frequently in the BAT than CFDC arm. Mortality results by pathogen showed an imbalance in *Acinetobacter* spp. infections (Table 2) with a higher rate in the CFDC arm than BAT arm. ICU and shock at randomization were more frequent in the CFDC arm than in the BAT arm in *Acinetobacter* spp. infections (Table 2). No safety concerns related to CFDC emerged.

Table 1. Baseline demographics and characteristics (CR-MITT population)

Table 1. Baseline demographics and characteristics (CR-MITT population)		
Parameter	**Cefiderocol (N=80)**	**BAT (N=38)**
Age, years		
Median (range)	69.0 (19–92)	62.0 (19–92)
≥65 years, n (%)	50 (62.5)	17 (44.7)
Male sex, n (%)	55 (68.8)	29 (76.3)
Creatinine clearance, median (range), mL/min	59.2 (9–540)	69.4 (5–271)
Creatinine clearance renal grading group, n %		
30–50 mL/min (moderate)	18 (22.5)	6 (15.8)
<30 mL/min (severe)	15 (18.8)	3 (7.9)
Clinical diagnosis at baseline, n (%)		
Nosocomial pneumonia*	40 (50.0)	19 (50.0)
BSI/Sepsis	23 (28.8)	14 (36.8)
cUTI	17 (21.3)	5 (13.2)
Most common Gram-negative pathogens isolated at baseline, n (%)		
Acinetobacter baumannii	37 (46.3)	17 (44.7)
Klebsiella pneumoniae	32 (40.0)	12 (31.6)
Pseudomonas aeruginosa	17 (21.3)	11 (28.9)
Empiric treatment failure, n (%)	46 (57.5)	22 (57.9)
ICU admission, n (%)	52 (65.0)	19 (50.0)
Shock, n (%)	17 (21.3)	6 (15.8)
ICU: intensive care unit; * includes hospital-acquired, ventilator-associated, and healthcare-associated pneumonia.		

Figure. CREDIBLE-CR study primary efficacy endpoints and secondary outcomes at test-of-cure visit in CR-MITT population.

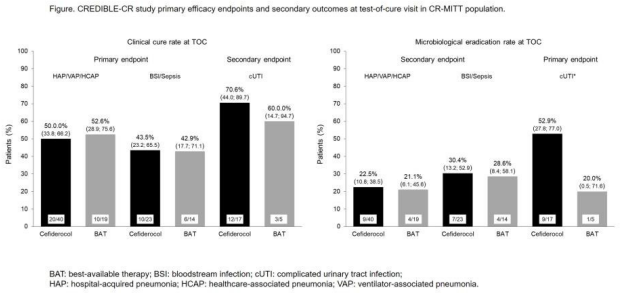

Table 2. All-cause mortality by baseline pathogen inpatients with or without Acinetobacter spp. infection (safety population)

Table 2. All-cause mortality by baseline pathogen inpatients with or without *Acinetobacter* spp. infection (safety population)			
		Cefiderocol (N=101)	**BAT (N=49)**
Mortality by species, n/N (%)			
All *Acinetobacter* spp.*		21/42 (50.0)	3/17 (17.6)
Acinetobacter baumannii		19/39 (48.7)	3/17 (17.6)
Klebsiella pneumoniae	with *Acinetobacter* spp.	8/34 (23.5)	4/16 (25.0)
	without *Acinetobacter* spp.	6/28 (21.4)	4/15 (26.7)
Pseudomonas aeruginosa	with *Acinetobacter* spp.	6/17 (35.3)	2/12 (16.7)
	without *Acinetobacter* spp.	2/11 (18.2)	2/11 (18.2)
Escherichia coli	with *Acinetobacter* spp.	1/6 (16.7)	0/3 (0.0)
	without *Acinetobacter* spp.	0/3 (0)	0/1 (0.0)
Baseline clinical characteristics and mortality overall with or without *Acinetobacter* spp. infection, n (%)			
With *Acinetobacter* spp.		N=42	N=17
Age ≥65 years		26 (61.9)	7 (41.2)
ICU		34 (81.0)	8 (47.1)
Ongoing shock		8 (19.0)	1 (5.9)
Shock <31 days prior to randomization		11 (26.2)	1 (5.9)
Mortality		**21 (50.0)**	**3 (17.6)**
Without *Acinetobacter* spp.		N=59	N=32
Age ≥65 years		38 (64.4)	15 (46.8)
ICU admission		23 (39.0)	13 (40.6)
Ongoing shock		4 (6.8)	4 (12.5)
Shock <31 days prior to randomization		8 (13.6)	5 (15.6)
Mortality		**13 (22.0)**	**6 (18.8)**
ICU: intensive care unit. *Includes *A. baumannii*, *A. nosocomialis*.			