Assessing the Real-world Clinical Outcomes of Patients Treated with Eravacycline for Complicated Intra-abdominal Infections

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Background

- Eravacycline (ERV) is a novel fluorocycline of the tetracycline (TET) class approved by the Food and Drug Administration (FDA) for treatment of complicated intra-abdominal infections (cIAIs) due to various infections[1-3]
- Although clinical experience with ERV is accumulating, limited data exist that describe the clinical and microbiological features associated with its use for cIAI beyond what was reported in randomized clinical trials (RCT)
- Real-world studies are critical as they evaluate the effectiveness, clinical profile and adverse events of the studied drug beyond the controlled conditions reported in RCTs
- Strengths of real-world studies include inclusion of high-risk patients, elderly, those with augmented renal clearance and multiple infection sources
- The purpose of this study was to evaluate the efficacy and safety of ERV for cIAI in the real-world setting

Methods

- This was a multicenter, retrospective, observational analyses conducted at 17 geographically distinct medical centers in the United States between September 2018 and November 2021
- We included patients 1) ≥18 years, 2) received ≥72 hours of ERV for any indication, 3) presumed source of infection is intra-abdominal
- We excluded 1) pregnant women, 2) prisoners
- Patients with more than one type of infection were allowed
- Primary outcome was clinical success defined as 30-day survival
- Secondary outcomes include, lack of 30-day infection-recurrence, no persistence of signs and symptoms while on ERV, adverse events and length of hospital stay
- All clinical outcomes were measured from time of the first ERV dose
- Combination therapy was defined as receiving any concomitant antimicrobial for the ERV-targeted infection for ≥48 hours
- Active antibiotic therapy was defined as receiving any antimicrobial for the ERV-targeted infection with or without evident in vitro data
- Hospital acquired infections were defined as infections acquired after 48 hours of hospital admission
- Intensive care unit (ICU) patients were defined as those whose index culture was measured during ICU admission
- Disease related markers were measured and severity of illness was estimated using the Charlson Comorbidity Index (CCI) and Acute Physiology and Chronic Health Evaluation (APACHE II) Score
- Descriptive analysis were performed using median (interquartile ranges) for continuous variables and numbers and proportions for nominal variables using SPSS statistics, IBM SPSS software, version 28.0 (IBM Corp., Armonk, NY).

Results

Table 1. Eravacycline Treatment Course Information

Criteria	Patients (n=96)
ERV dose	
1 mg per kg	90 (93.8)
Common ERV frequency	
Every 12 hours	86 (89.6)
Every 12 hours on day 1, then q24 hours	6 (6.3)
ERV Duration, days	8.6 [4.4 –19.4]
ERV Start from culture, days[1]	4.2 [1.9 – 8.5]
IV Combination therapy, any	23 (33.1)
Meropenem	6 (6.3)
TMP –SMX	4 (4.1)
IV Active therapy before ERV, any	50 (52.1)
Cefepime	8 (8.3)
Ceftazidime/avibactam	6 (6.3)
Ertapenem	7 (7.3)
Daptomycin	6 (6.3)
Meropenem	15 (15.6)
Piperacillin-tazobactam	14 (14.6)
Linezolid	9 (9.4)
Vancomycin	19 (19.8)

All data demonstrated as median (interquartile range) or n (percentage)
Abbreviations: TMP-SMX: Trimethoprim-sulfamethoxazole
1: only among those with positive cultures (n=85)

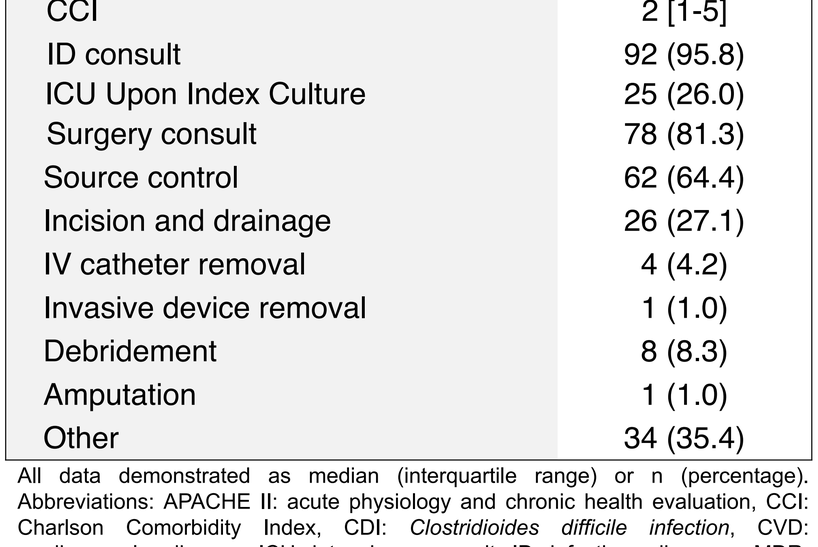
Results

Table 2. Baseline Clinical Criteria of Patients Treated

Criteria	Patients (n=96)
Age, years	59.5 [47.0-67.0]
Sex, male	53 (55.2)
Race, Caucasian	60 (62.5)
Race, African American	17 (17.7)
BMI	27.5 [23.5 – 33.5]
Weight, kg	80.6 [63.9 – 97.5]
Comorbid conditions	
Acute kidney injury	72 (22.7)
CVD	42 (13.2)
Chronic dialysis	21 (6.6)
CDI	23 (7.3)
Connective tissue disease	20 (6.3)
Dementia	11 (3.5)
Diabetes	22 (22.9)
Heart failure	62 (19.6)
Immunosuppression factors	27 (28.1)
Tumor	12 (12.5)
Liver disease	26 (27.1)
Obese	36 (37.5)
Peptic ulcer disease	12 (3.8)
None	44 (13.9)
MDR risk factors[1]	
Antimicrobials in <90 days	51 (53.1)
Colonization with resistant organisms	9 (9.4)
Hospitalization> 48 hours	54 (65.3)
Prior infection with resistant infection	13 (13.5)
Surgery in 30 days before index	33 (34.4)
Other Sources of infection	6 (6.2)
Hepatic abscess	1 (1.0)
Pneumonia	4 (4.1)
Skin and soft tissue	1 (1.0)
Disease related risk factors	
APACHE II score	14 [9-19]
Blood culture positive	21 (21.9)
CCI	2 [1-5]
ID consult	92 (95.8)
ICU Upon Index Culture	25 (26.0)
Surgery consult	78 (81.3)
Source control	62 (64.4)
Incision and drainage	26 (27.1)
IV catheter removal	4 (4.2)
Invasive device removal	1 (1.0)
Debridement	8 (8.3)
Amputation	1 (1.0)
Other	34 (35.4)

All data demonstrated as median (interquartile range) or n (percentage). Abbreviations: APACHE II: acute physiology and chronic health evaluation, CCI: Charlson Comorbidity Index, CDI: *Clostridioides difficile infection*, CVD: cardiovascular disease, ICU: intensive care unit, ID: infectious diseases, MDR: multi-drug resistant. [1]MDR risk factors include the ones listed in addition to colonization with resistant organisms, home wound care, admitted from nursing home or extended care facility, surgery in past 30 days before index culture.

Figure 1. Common Reason to Select Eravacycline



Abbreviations: CDI: *Clostridioides difficile* associated diarrhea, CRE: Carbapenem-resistant Enterobacterales, PO: oral

Results

Figure 2. Pathogens Targeted

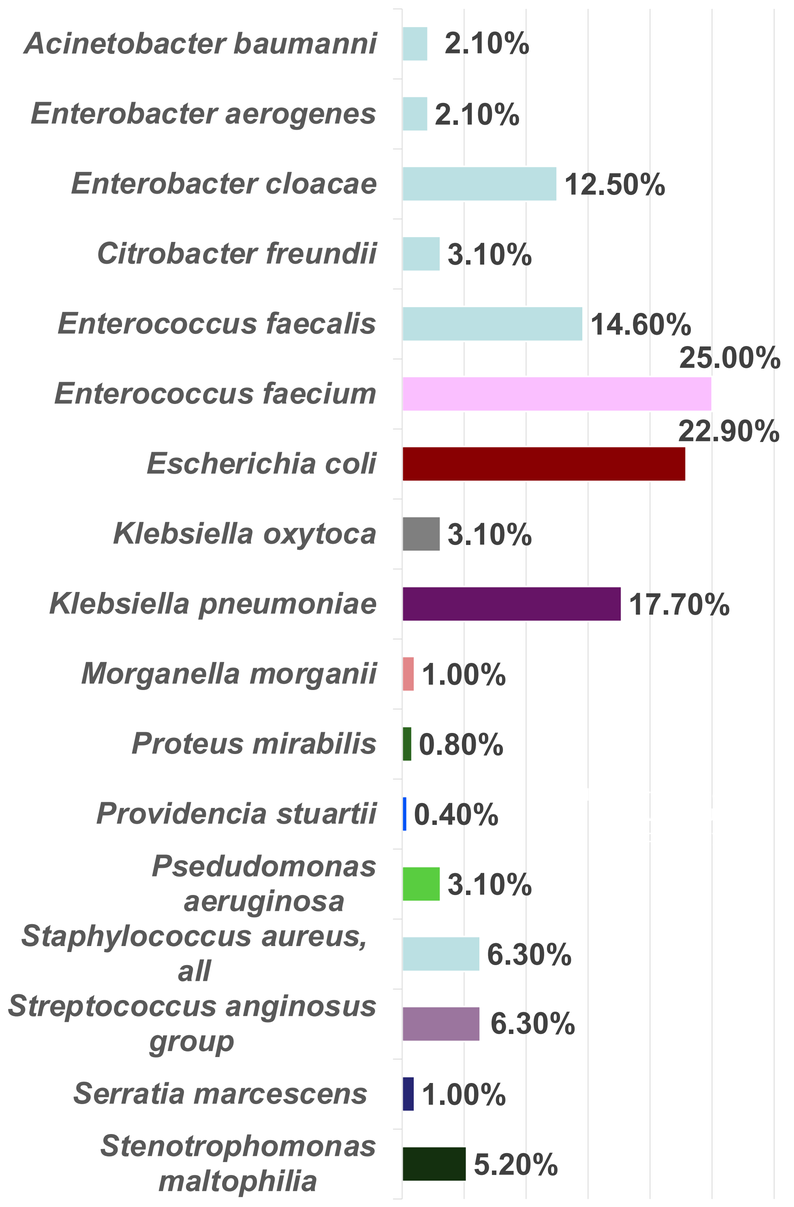


Table 3. Clinical Outcomes and Adverse Events

Criteria	Patients (n=96)
Clinical Outcomes[1]	
30-day mortality	22 (22.9)
Infection related mortality	16 (16.7)
30-day recurrence	5 (5.2)
No resolution of signs/symptoms	4 (4.2)
Switch to another agent	25 (26.0)
Switch to an oral agent	13 (13.5)
Length of stay, days	27 [13.0 – 48.3]
Adverse events, any	6 (6.3)
Gastrointestinal	5 (5.2)
Hepatotoxicity	1 (1.0)
Led to drug discontinuation	4 (4.1)

All data demonstrated as median (interquartile range) or n (percentage)
[1] From ERV start date

Conclusions

- Our report offers new insights into patients that are typically excluded from RCTs, those with comorbidities, previous antibiotic use, and MDR pathogens
- The most common pathogens when ERV was used for cIAI were En*terococcus faecium* and *Escherichia coli*, respectively
- Collectively, ERV in the real-world setting was associated with positive clinical outcomes that are comparable to RCT results
- Comparative studies investigating factors associated with clinical success are crucial for optimal antibiotic selection
- Larger prospective real-world studies investigating factors associated with clinical success in cIAI are essential

References

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Disclosures

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- This study was presented in part in Alosaimy S, Molina KC, Claeys KC, et al. Open Forum Infect Dis. 2020;7(5):ofaa071.