Real World Multi-center Experience with Eravacycline for Complicated Infections

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Background

- Eravacycline (ERV) is a novel fluorocycline of the tetracycline (TET) class which was approved by the Food and Drug Administration (FDA) in August 2018 for treatment of complicated intra-abdominal infections (cIAIs) following the IGNITE1 and IGNITE4 trials[1-2]
- ERV has demonstrated potent *in vitro* activity against most Gram-positive and Gram-negative pathogens, including carbapenem-resistant Enterobacterales (CRE) and *A. baumannii,* and was generally well tolerated in clinical trials, with gastrointestinal (GI) disturbances being the most common adverse events (AEs)[3-4]
- It has a unique potential role in patients with multidrug-resistant (MDR) organisms, allergies to ß-lactams, and/or if *Clostridioides difficile* infection (CDI) is present or of concern[3-4]
- We aimed to explore the clinical and safety outcomes among patients treated with ERV in the real-world setting

Methods

- A multicenter, retrospective observational study conducted at (n=15) geographically distinct medical centers in the United States between November, 2018 and August, 2020
- We included patients (≥18 years), who received ≥72 hours of ERV for any indication
- Exclusion criteria: pregnancy, prisoners, missing data
- Primary outcome was 30-day survival
- Secondary outcomes included absence of 30-day recurrence, resolution of signs and symptoms while on ERV and 90-day survival
- All clinical outcomes were measured from time of the first ERV dose
- 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
- Nosocomial infections were defined as those with positive index cultures ≥48 hours after hospital admission
- Combination therapy was defined as receiving any concomitant antimicrobial for ERV-targeted infection for ≥48 hours
- 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 26.0 (IBM Corp., Armonk, NY)

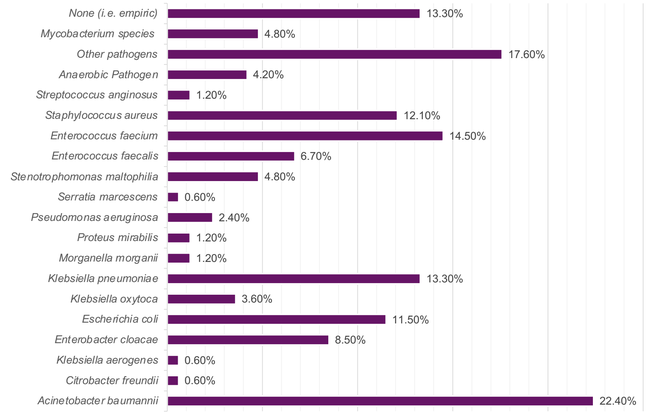
Results

Table 1. Baseline criteria

Characteristics	Results (n=165)
Age, years	61.0 (50.5-69.5)
Age ≥ 65 years	67 (40.6)
Sex, male	91 (55.2)
Race, Caucasian	98 (59.4)
Comorbid conditions	139 (84.2)
Chronic dialysis	13 (7.9)
Diabetes	65 (39.4)
Heart failure	35 (21.2)
History *Clostridioides difficile* associated diarrhea	13 (7.9)
Immunosuppressed	26 (15.8)
Liver disease	24 (14.5)
Disease related risk factors	
APACHE II score	14.0 (10.0 – 20.2)
CCI	3.0 (1.5 – 5.5)
Combination therapy	93 (56.4)
ID consult	156 (94.5)
Mechanically ventilated	25 (15.2)
Nosocomial infections[1]	79 (55.2)
Surgery consult	82 (49.7)
MDR risk factors[2]	146 (88.5)
Antimicrobials in past 90 days	96 (58.2)
Hospitalization in past 90 days	94 (57.0)
Prior infection with resistant organisms	47 (28.5)
Infection source	
Bone and joint	12 (7.3)
Intraabdominal	41 (24.8)
Primary bacteremia	12 (7.3)
Respiratory tract	43 (26.1)
Skin and soft tissue	28 (17.0)
Other[3]	20 (12.1)
Unknown	9 (5.5)

All data demonstrated as median (interquartile range) or n (percentage). APACHE II: acute physiology and chronic health evaluation, CCI: Charlson Comorbidity Index, CKD: chronic kidney disease, ICU: intensive care unit, ID: infectious diseases. [1]Noscomial infections measured among those with a documented positive culture (n=143). [2]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. [3]Other sources of infection include urinary tract infections (n=6), invasive prosthetic device (n=5), infective endocarditis (n=1), others (n=8).

Figure 1. Pathogens targeted



*Pathogens targeted were based on clinician's note. Eravacycline may have been used for more than one pathogen.
Mycobacterium species: *Mycobacterium abscessus* (n=7), *Mycobacterium chelonae* (n=1)

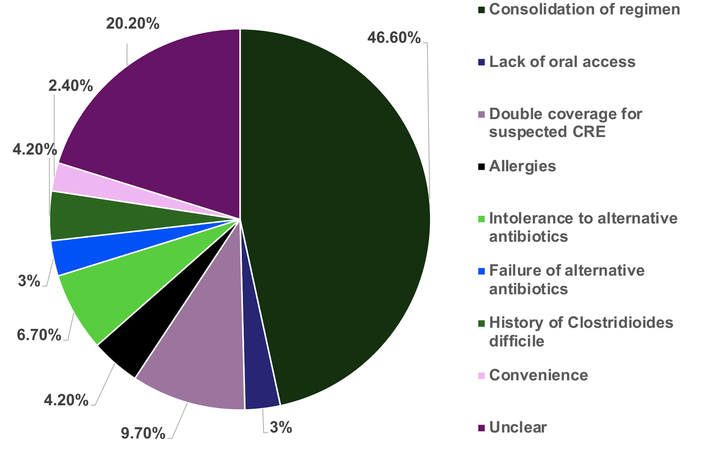
Table 2. Clinical and Safety Outcomes

Outcome	Results (n=165)
Efficacy	
30-day survival	132 (80.0)
90-day survival	117 (70.1)
Resolution of signs and symptoms of infection	120 (72.7)
Lack of 30-day recurrence	153 (92.7)
Safety	
Any adverse event	20 (12.1)
Gastrointestinal	11 (6.7)
Hepatotoxicity	4 (2.4)
Nephrotoxicity	2 (1.2)
Dermatological reaction	1 (0.6)
Led to drug discontinuation	6 (3.6)

Nephrotoxicity defined as serum creatinine increase by 50% from baseline and ≥ 0.5 mg/dL on two consecutive measures.
Hepatotoxicity defined as at least one increase in AST or ALT levels. All data demonstrated as n (percentage)

Results

Figure 2. Rationale for eravacycline selection



Conclusions

- We present the largest early real-world multicenter experience to date evaluating ERV use in various infections across geographically distinct medical centers in the United States
- Positive clinical outcomes had been demonstrated in the majority of ERV treated patients and well-tolerated with no incidences of *Clostridioides difficile* associated diarrhea
- Larger prospective real-world studies are essential to further confirm our early clinical findings

References

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Disclosures

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