Early Real-World Evidence in the Use of Eravacycline for the Management of Draconian Infections

Amy L. Carr, PharmD[1]; Amer El Ghali, PharmD, PGY1 Resident[2,3]; Parminder Kaur[3]; Sarah B. Minor, PharmD[1]; Anthony M. Casapao, PharmD, MPH[3]
[1]AdventHealth Orlando; [2]Memorial Hospital West; [3]University of Florida College of Pharmacy

AdventHealth Pharmacy

UF College of Pharmacy UNIVERSITY of FLORIDA

Abstract (updated)

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 45 patients, 53.3% were males with a mean age of 53 ±18.3 years and mean body weight of 76.1 ±26.1 kg. Mean APACHE II and Charlson scores were 18.5 (±7.2) and 4.9 (±2.8), respectively. 73% received ERV for an off-label indication or organism. Infection types were respiratory (47%), cIAI (31%), SSTI (11%), UTI (2%) and other (9%). 89% of patients had positive cultures, while 53% were treated as a polymicrobial infection and 13% 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*. 69% were given another antibiotic prior to ERV with a median duration of 8.5 (4-14.5) days. Median duration of ERV was 8 (5-11) days. 60% 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, 20% continued ERV. Clinical success was observed in 73% (32/45) of patients. Clinical outcome by infection type is summarized in Figure 1. Of 13 cases of clinical failure, 54% were changed to alternative, 38% died while on ERV, and 31% failed to resolve signs/symptoms.

Background

- Eravacycline (ERV) is a next generation tetracycline that has US FDA approval for complicated intra-abdominal infections (cIAI) and has *in vitro* activity to multi-drug resistant organisms (MDRO)
- There has been an increased prevalence of MDROs in the past three decades with limited treatment modalities allowing for ERV's potential use
- IGNITE1 and IGNITE4 trials had limitations and data is sparse outside the US FDA indications
- The purpose was to describe the utility of ERV in real-world clinical practice.

Methods

Study Design: Multi-site, retrospective case series of patients admitted to AdventHealth Central Florida from November 2018 to September 2019. Data was extracted from EHR.
Inclusion Criteria: Patients ≥ 18 years of age, ≥ 2 doses of ERV, and an indication for treatment.
Primary endpoint:

Clinical Success (resolution of ≥ 2)	Clinical Failure
Resolution of Fever: Temperature < 100.4 °F Resolution of leukocytosis: <11,000 cells/mm^3 Negative blood culture	Death during hospitalization Therapy switch from ERV to alternative agent No resolution of ≥2 symptoms

Secondary endpoints: Hospital readmission at 30 days and 30-day all-cause mortality.
Adjudication: Cases were screened and reviewed by two separate investigators and then adjudicated by an independent reviewer.

Results

Table 1: Characteristics of Patients at Baseline

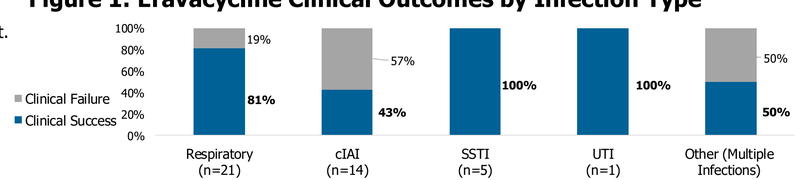
Patient Characteristic	Full Cohort (n=45)	US FDA Indicated (n=12)	Off-label Indication (n=33)	Monomicrobial Infection (n=16)	Polymicrobial Infection (n=24)	Combination therapy (n=27)
Age, years	53.2 ±18.3	61.4 ± 12.8	50.2 ± 19.2	52.4 ± 20.3	54.5 ± 17.4	49.1 ± 20.6
Male Gender	24 (53.3)	7 (58.3)	17 (51.5)	8 (50.0)	15 (62.5)	13 (48.1)
Race						
Caucasian	36 (80.0)	9 (75.0)	28 (84.8)	12 (75.0)	20 (83.3)	20 (74.1)
African American	5 (11.1)	2 (16.7)	3 (9.09)	3 (18.8)	1 (4.2)	4 (14.8)
Actual Body Weight, kg	76.1 ± 26.6	76.7 ± 19.4	75.9 ± 29.1	76.7 ± 33.0	77.9 ± 24.0	66.4 ± 21.5
APACHE II Score	18.5 ± 7.2	17.9 ± 8.8	18.5 ± 6.7	17.25 ± 6.0	18.58 ± 7.6	19.85 ± 7.7
Charlson Comorbidity Index Score	4.9 ± 2.8	5.58 ± 3.0	4.9 ± 2.7	4.25 ± 2.7	5.38 ± 2.9	4.48 ± 2.9
Previous Hospitalization, One Year Prior	38 (84.4)	12 (100.0)	29 (87.9)	14 (87.5)	22 (91.7)	25 (92.6)
Previous Surgery, 30-days	15 (33.3)	6 (50.0)	11 (33.3)	2 (12.6)	14 (58.3)	11 (40.7)
Prosthetic device/hardware	9 (20.0)	3 (25.0)	7 (21.2)	2 (12.6)	6 (25)	4 (14.8)
Diabetes	20 (44.4)	6 (50.0)	16 (48.5)	8 (50.0)	14 (58.3)	12 (44.4)
Liver disease	5 (11.1)	3 (25.0)	4 (12.1)	2 (12.6)	5 (20.8)	6 (22.2)
Previous carbapenem use, 30 days prior	11 (24.4)	5 (41.7)	9 (27.3)	3 (18.8)	9 (37.5)	7 (25.9)
Previous cefepime use, 30 days prior	7 (15.6)	3 (25.0)	6 (18.2)	3 (18.8)	4 (16.7)	5 (18.5)
Previous tigecycline use, 30 days prior	2 (4.4)	0 (0.0)	2 (6.1)	1 (6.3)	1 (4.2)	2 (7.4)
Positive cultures	40 (88.9)	10 (83.3)	30 (90.9)	16 (100)	24 (100)	22 (81.5)

Continuous variables are presented as mean ± standard deviation. Categorical data is presented as n(%)

Outcomes of the Full Cohort (n=45)

- Overall, 71% (32/45) had clinical success and 29% (13/45) had clinical failure

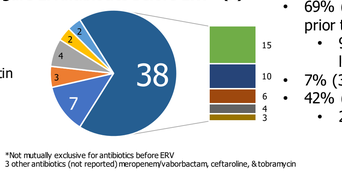
Figure 1: Eravacycline Clinical Outcomes by Infection Type



- 20% (9/45) 30-day all-cause mortality
- 36% (16/45) patients had readmission within 30 days

Prescribing Full Cohort (n=45)

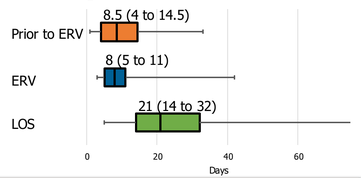
Figure 2. Antibiotics Before ERV* (n)



*Not mutually exclusive for antibiotics before ERV
3 other antibiotics (not reported) meropenem/vaborbactam, ceftaroline, & tobramycin

- 69% (31/45) received an antibiotic prior to ERV
  - 97% (30/31) received a beta-lactam
- 7% (3/45) had an ADE while on ERV
- 42% (19/45) discharged on antibiotics
  - 20% (9/45) continued ERV

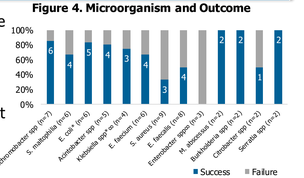
Figure 3. Duration of Outcomes



Microbiology Full Cohort (n=45)

- 89% (40/45) had positive cultures
- 57% (37/64) of isolates were gram negative
- 22% (10/40) of patients has carbapenem resistant infections
- 15 isolates had available ERV MIC data

Figure 4. Microorganism and Outcome

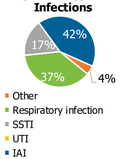


Not mutually exclusive for positive cultures. *one isolate was ESBL (each) and m-one isolates was KPC (each) producing

Polymicrobial (n=24)

- 58% of polymicrobial infections had clinical success
- 2/6 *S. maltophilia* were polymicrobial
- 6/7 *Achromobacter spp.* were polymicrobial
- 6/6 *E. coli* were polymicrobial
- 38% (9/24) had *S. aureus* (5/9) were MRSA
- 25% (6/24) had *E. faecium* (3/6) were VRE

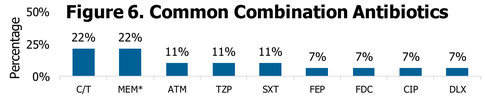
Figure 5. Types of Infections



Combination Therapy (n=27)

- 60% (27/45) received ERV with another antibiotic
  - 85% (23/27) received a beta-lactam with ERV
- 67% (18/27) received combination therapy had clinical success

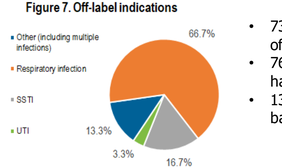
Figure 6. Common Combination Antibiotics



Not mutually exclusive for combination therapy. *one patient received meropenem/vaborbactam

Off-Label Indications (n=33)

Figure 7. Off-label indications



- 73% (33/45) received ERV for off-label use
- 76% (25/33) of off-label use had clinical success
- 13% (6/45) patients had bacteremia

Conclusion

- Initial real-world experience with ERV differs significantly from the trials regarding severity of illness, types of infection, and clinical outcomes
- Primarily used as a salvage agent for the management of severe infections after failure from several beta-lactam therapy
- Further evaluation is necessary for using ERV as combination therapy and in off-label indications

References

1.Eravacycline [package insert]. Watertown, MA: Tetraphase Pharmaceutical, Inc.; 2018.
2.Solomkin, Joseph, et al. "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." *JAMA surgery* 152.3 (2017): 224-232.
3.Solomkin, Joseph S., et al. "IGNITE4: Results of a Phase 3, Randomized, Multicenter, Prospective Trial of Eravacycline vs Meropenem in the Treatment of Complicated Intraabdominal Infections." *Clinical Infectious Diseases* (2018).

Disclosures

All authors of this presentation have nothing to disclose and no funding source had any involvement in this work.