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ORIGINAL RESEARCH

Eravacycline Treatment for Carbapenem-Resistant *Acinetobacter baumannii* in Lung Transplant Recipients: A Real-World Retrospective Study

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Background: Carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections were associated with higher mortality and significant healthcare burden. Novel antibiotics provided a powerful weapon against CRAB. This study aimed to describe the effectiveness of eravacycline for the treatment of CRAB infections in lung transplant recipients.

Methods: This was a single-center, retrospective study that enrolled lung transplant recipients with CRAB infections who received eravacycline for over 72 hours between August 2023 and December 2024. The primary outcome was 28-day survival rate. Secondary outcomes included 14-day survival and clinical failure rate.

Results: A total of 24 lung transplant recipients were enrolled, with a median age of 60.5 years and a predominance of male patients. Nearly half had interstitial lung disease as the primary pulmonary condition. These recipients in our study mainly had pulmonary infections attacked by CRAB, with six individuals suffering septic shock. The median duration of eravacycline therapy was 10 days, with most patients receiving combination therapy. The primary outcome, the 28-day survival rate, was 83.3%, while the secondary outcomes showed a 14-day survival rate of 100% and a clinical failure rate of 37.5%. The median ICU and hospital lengths of stay were 12.5 and 55 days, respectively. A comparison between patients with and without clinical failure showed that those with clinical failure were older, had a higher incidence of septic shock, a higher proportion of continuous renal replacement therapy, and a longer ICU stays. Additionally, these patients exhibited an elevated heart rate, higher levels of ALT and AST, lower protein levels (total protein, albumin), prolonged PT and APTT, and increased level of CRP and PCT at the end of treatment.

Conclusion: This study presented the clinical efficacy of eravacycline in lung transplant recipients with CRAB infections, providing valuable evidence and clinical experience for its use in organ transplant populations.

Keywords: carbapenem-resistant *Acinetobacter baumannii*, eravacycline, lung transplantation, effectiveness

Introduction

Carbapenem-Resistant *Acinetobacter baumannii* (CRAB) infections are one of the major public health "threats" of the 21st century, with fluctuating antimicrobial resistance rates, presenting significant challenges to healthcare institutions. In the 2019 global burden of antimicrobial resistance (AMR), *Acinetobacter baumannii* ranked as the fifth leading pathogen causing infection-related deaths.[1] This bacterium has a remarkable ability to acquire resistance and undergo clonal transmission, as well as the capacity to evade host immunity and persist in the environment, which facilitates its spread in healthcare settings.[2] As a result, CRAB is considered by the World Health Organization (WHO) as a priority pathogen

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for the development of novel antibiotics.[3] However, it is critical to highlight that the treatment of CRAB infections presents significant challenges. First, CRAB is typically isolated from respiratory or wound specimens, and distinguishing between infection and colonization is not straightforward, particularly in patients with immunodeficiencies or other high-risk conditions, such as transplant recipients, cancer patients, or those undergoing corticosteroid therapy.[4] Secondly, it is crucial to recognize that carbapenem resistance is often associated with resistance to multiple other classes of antibiotics, leading to multidrug resistance (MDR) or even extensively drug-resistant (XDR) phenotypes.[5] As a result, when a strain of *Acinetobacter baumannii* is carbapenem-resistant, it is commonly resistant to other antimicrobial agents as well, limiting available therapeutic options. Additionally, the resistance mechanisms of *A. baumannii* are complex,[6,7] involving biofilm formation, overexpression of efflux pumps, acquisition of resistance, and modifications to the outer membrane. Biofilm formation associated with CRAB infections is often linked to both resistance phenotypes and increased virulence,[8] underscoring the importance of removing contaminated indwelling devices.[9] Recent studies have highlighted the molecular mechanisms behind colistin resistance in CRAB, particularly the addition of phosphoethanolamine to lipid A, contributing to membrane modifications that reduce colistin efficacy.[10,11] Lung transplant recipients, as a high-risk population for infections, are particularly vulnerable to CRAB and other drug-resistant pathogens due to factors such as impaired host immunity, ciliary clearance dysfunction, the presence of invasive devices, and ICU admission. Managing infections in this population is extremely challenging, and effective treatment strategies are urgently needed.

For CRAB infections, available treatment options and clinical data are limited,[4] with current therapies primarily relying on tetracyclines such as tigecycline, sulbactam and its combinations, and polymyxin antibiotics.[5] With the continuous advancement of global drug development, new antimicrobial agents have emerged in recent years, and innovative drugs will provide new solutions for clinical management of resistance, particularly for the treatment of infections caused by resistant bacteria. Eravacycline is a novel synthetic fluorocycline antibiotic that is not affected by resistance mechanisms involving tetracycline efflux pumps or ribosomal protective proteins.[12,13] It provides broad-spectrum coverage against common Gram-negative bacteria (including Acinetobacter baumannii), Gram-positive bacteria, anaerobes, and atypical pathogens, and is effective against MDR bacteria mediated by various resistance mechanisms.[14–16]

Both in vitro and in vivo studies have shown that eravacycline has stronger antibacterial activity against Carbapenem-resistant *Enterobacteriaceae* (CRE) and CRAB compared to tigecycline, achieves higher concentrations in lung tissues, and has fewer adverse effects, making it a superior alternative option over tigecycline.[12] Additionally, studies have demonstrated that eravacycline, when combined with with β-lactams or polymyxin B exhibits synergistic effects against clinically common carbapenem-resistant Gram-negative bacteria.[17] Phase II and III clinical trials have confirmed that eravacycline is non-inferior to ertapenem and meropenem in the treatment of complicated intra-abdominal infections (cIAI).[18–20] In real-world studies, eravacycline has shown good efficacy and safety in treating intra-abdominal infections, pneumonia, bone and joint infections, skin and soft tissue infections, and bloodstream infections.[21,22] However, current clinical data on the use of eravacycline for treating CRAB infections in organ transplant population remain limited, and further real-world studies are needed. Therefore, this study aims to describe the early clinical experience with this novel antibiotic for CRAB infections in lung transplant recipients, providing more treatment options and better clinical decision-making for managing resistant bacteria infections.

Methods

Study Design and Participants

This was a real-world, single-center, retrospective study conducted in China from August 2023 to December 2024. The study included (1) patients aged over 18 years, (2) lung transplant recipients with CRAB infections, and (3) eravacycline treatment for more than 72 hours. The exclusion criteria for this study were: (1) age < 18 years, (2) eravacycline treatment for less than 72 hours, (3) patients who underwent re-transplantation, (4) colonization or contamination of sample, (5) pregnant or breastfeeding women, and (6) patients with incomplete clinical data. The patients in the study were administered eravacycline according to the dosage and usage recommended in the product's prescribing

information. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Zhejiang University (approval number: 2025–0212), and was conducted in accordance with the Declaration of Helsinki. Due to the retrospective nature of this study and anonymization of the data, the informed consent was waived. The organs transplanted for the lung transplant recipients were voluntarily donated by donors, and both organ donation and transplantation were conducted in compliance with the Declaration of Istanbul.

Basic demographic data (age, sex, body mass index (BMI)), clinical information (underlying lung disease, comorbidities, ICU admission), surgical variables (surgical type, duration, intraoperative blood loss, blood transfusion, extracorporeal membrane oxygenation (ECMO) support), perioperative monitoring (APACHE II score, SOFA score, extubation time, reintubation, tracheostomy, acute kidney injury (AKI), liver dysfunction, cerebrovascular disease, continuous renal replacement therapy (CRRT), etc), antimicrobial susceptibility test results of the isolated strains, and eravacycline treatment details (initiation timing, prior antibiotic use, course of therapy, combination therapy, vital signs and laboratory results before and after treatment, etc) were collected from electronic medical records. The primary outcome of this study was the 28-day survival rate. Secondary outcomes included 14-day survival and clinical failure rate. Other outcome variables included length of ICU stay and hospital stay.

Definition

The diagnosis of acute kidney injury was conducted according to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines,[23] and septic shock was diagnosed based on the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).[24] Variables included the APACHE II score and the oxygenation index, recorded as the worst values within the first 24 hours after ICU admission post-surgery. The SOFA score was calculated using the standard scoring system to assess the severity of organ dysfunction. Clinical failure was classified as the persistence of clinical symptoms and signs from baseline to the end of treatment, without clinical resolution or improvement.[25,26]

Statistical Analysis

Categorical variables were expressed as frequencies and percentages. Group differences for categorical variables were evaluated using the Chi-square test. For continuous variables that followed a normal distribution, data were presented as the mean and standard deviation, with group differences evaluated using Student's *t*-test. In contrast, continuous variables that did not follow a normal distribution were represented by the median and interquartile range (IQR), with group differences analyzed using the Mann–Whitney *U*-test. Statistical analysis was performed using IBM SPSS Statistics v.25.0.

Results

Baseline Characteristics

A total of 24 eligible patients were included in this study, with their characteristics summarized in Table 1. The median age of the patients was 60.5 years, with 79.2% being male. Among these lung transplant recipients, the primary lung disease was predominantly interstitial lung disease (45.8%), followed by chronic obstructive pulmonary disease (25%), obliterative bronchiolitis (20.8%), and bronchiectasis (8.3%). Comorbidities in these recipients included hypertension (12.5%), diabetes (20.8%), cardiovascular disease (16.7%), cerebrovascular disease (8.3%), gastrointestinal disease (8.3%), connective tissue disease (12.5%) and other chronic disease. Five patients (20.8%) were admitted to the ICU for monitoring and management before transplantation.

Intraoperative and Postoperative Management

Among these lung transplant recipients, the majority (95.8%) underwent bilateral lung transplantation, with an average surgical duration of 7.54 hours. The median intraoperative blood loss was 800 mL, and the median volume of red blood cell transfusion during surgery was 400 mL. The majority of patients (83.3%) received ECMO support during the procedure. In the postoperative intensive care, the average APACHE II and SOFA scores were 19.08 and 9.21, respectively. The median worst oxygenation index within the first 24 hours of ICU admission was 210.5. A significant

Table 1 The Clinical Characteristics of Lung Transplant Recipients Treated with Eravacycline for CRAB Infections

Characteristic	Overall (n = 24)
Male sex	19 (79.2%)
Age, years	60.50 (43.25–66.50)
BMI (Kg/m^2)	18.78 ± 4.56
Native pulmonary disease	
Interstitial lung disease	11 (45.8%)
Chronic obstructive pulmonary disease	6 (25.0%)
Bronchiolitis obliterans syndrome	5 (20.8%)
Bronchiectasis	2 (8.3%)
Comorbidities	
Hypertension	3 (12.5%)
Diabetes	5 (20.8%)
Cardiovascular disease	4 (16.7%)
Cerebrovascular disease	2 (8.3%)
Gastrointestinal disease	2 (8.3%)
Chronic liver disease	1 (4.2%)
Chronic kidney disease	1 (4.2%)
Connective tissue disease	3 (12.5%)
ICU admission before operation	5 (20.8%)
Lung transplantation	
Type of transplant	
Bilateral	23 (95.8%)
Single	1 (4.2%)
Duration of operation, days	7.54 ± 1.63
Intraoperative bleeding volume, mL	800 (600–1210)
Intraoperative red blood transfusion volume, mL	400 (0–1275)
ECMO support	20 (83.3%)
Perioperative intensive care	
APACHE II score	19.08 ± 4.86
SOFA score	9.21 ± 2.78
Oxygenation index	210.5 (164–350)
Extubation within 72 hours after operation	18 (75.0%)
ECMO supporting time, hours	21.00 (17.25–35.50)
Re-intubation	7 (29.2%)

(*Continued*)

Table 1 (Continued).

Characteristic	Overall (n = 24)
Tracheotomy	7 (29.2%)
Acute kidney injury	13 (54.2%)
Liver dysfunction	13 (54.2%)
Postoperative cerebrovascular event	3 (12.5%)
Continuous renal replacement treatment	9 (37.5%)
Septic shock	6 (25.0%)

Abbreviations: CRAB, Carbapenem-resistant Acinetobacter baumannii; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; ECMO, extracorporeal membrane oxygenation;

proportion of patients (75%) had their endotracheal tubes removed within 72 hours postoperatively. For those who required ECMO support, the average duration of support was 21 hours. Throughout the treatment period, seven transplant recipients required reintubation to maintain respiratory function. Additionally, seven patients underwent tracheostomy due to difficulties weaning from the ventilator after transplantation. During the treatment period, 13 patients developed AKI, and 13 patients experienced liver dysfunction. Three patients suffered cerebrovascular events. Nine patients received CRRT in the ICU.

Among the 24 patients with CRAB infection, the primary infection site was the lungs. Six patients developed septic shock. Additionally, the details regarding in vitro susceptibilities were available in Table 2. Among these *A. baumannii* isolates, all were resistant to Imipenem, meropenem, ticarcillin-clavulanic acid, piperacillin-tazobactam and ciprofloxacin. Most isolates exhibited in vitro resistance to ceftazidime, cefepime, doxycycline, tobramycin, levofloxacin, and trimethoprim-sulfamethoxazole, with the resistance rates ranging from 65.2% to 95.7%. Susceptibility testing for cefoperazone-sulbactam showed that 17.4% of isolates were susceptible, while 39.1% were intermediately susceptible. Tigecycline susceptibility was assessed for 21 isolates, of which 9 (42.9%) were intermediately susceptible and 9

Table 2 In Vitro Susceptibilities of CRAB Isolates From Lung Transplant Recipients

Antibiotics	Isolates	Susceptible	Intermediate	Resistant
Imipenem	23	–	–	23 (100%)
Meropenem	23	–	–	23 (100%)
Cefepime	23	–	3 (13%)	20 (87%)
Ceftazidime	23	1 (4.3%)	–	22 (95.7%)
Ticarcillin-clavulanic acid	23	-	-	23 (100%)
Cefoperazone-sulbactam	23	4 (17.4%)	9 (39.1%)	10 (43.5%)
Piperacillin-tazobactam	23	-	-	23 (100%)
Ciprofloxacin	23	-	-	23 (100%)
Levofloxacin	23	-	6 (26.1%)	17 (73.9%)
Tobramycin	23	4 (17.4%)	1 (4.3%)	18 (78.3%)

(*Continued*)

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Table 2 (Continued).

Antibiotics	Isolates	Susceptible	Intermediate	Resistant
Trimethoprim-sulfamethoxazole	23	8 (34.8%)	-	15 (65.2%)
Doxycycline	23	3 (13.0%)	-	20 (87%)
Tigecycline	21	9 (42.9%)	9 (42.9%)	3 (14.2%)
Minocycline	23	11 (47.8%)	7 (30.4%)	5 (21.8%)
Colistin	23	23 (100%)	-	-

Abbreviation: CRAB, Carbapenem-resistant *Acinetobacter baumannii*;

(42.9%) were susceptible. Nearly half of isolates (47.8%) were susceptible to minocycline, with 30.4% showing intermediate susceptibility. Colistin susceptibility results were obtained for 23 isolates, all of which were susceptible.

Eravacycline Treatment Details and Outcomes

In this cohort (Table 3), the median duration of eravacycline therapy was 10 days, with the median time to initiate eravacycline therapy being 4.5 days. The majority of patients received eravacycline combination therapy, with the combined antimicrobial agents including cefoperazone-sulbactam, polymyxins, and carbapenems. Prior to starting

Table 3 The Treatment Details of Eravacycline for CRAB Infections in Lung Transplant Recipients

Eravacycline Treatment	Overall (n = 24)
Duration of eravacycline therapy, days	10.00 (7.00–13.75)
Time to treatment initiation, days	4.50 (1.25–9.50)
Combination therapy	
With a type of antibiotic	11 (45.8%)
With two types of antibiotics	8 (33.3%)
With three types of antibiotics	2 (8.3%)
Antibiotics used prior to eravacycline	
Cefoperazone-sulbactam	10 (41.7%)
Carbapenems	12 (50.0%)
Polymyxins	12 (50.0%)
Tigecycline	6 (25.0%)
Minocycline	3 (12.5%)
Pre-treatment parameters with eravacycline	
Vital signs	
Temperature, °C	37.0 (36.7–37.2)
Mean arterial pressure (MAP), mmHg	79 ± 10

(*Continued*)

Table 3 (Continued).

Eravacycline Treatment	Overall (n = 24)
Respiratory rate, breaths/min	21 ± 3
Heart rate, beats/min	106 ± 20
Laboratory results	
White blood cell counts, × 10^9/L	11.9 (8.5–15.7)
Neutrophil cell counts, × 10^9/L	10.20 (6.77–14.53)
Red blood cell counts, × 10^{12}/L	2.47 ± 0.46
Hemoglobin, g/L	80 ± 13
Platelet counts, × 10^9/L	85 (58–213)
ALT, U/L	22 (15–33.5)
AST, U/L	34.5 (25.25–51)
Total protein, g/L	61.5 ± 8.6
Albumin, g/L	39.8 ± 7.8
Total bilirubin (TBIL), μmol/L	16.8 (9.5–22.5)
Direct bilirubin (DBIL), μmol/L	3.4 (2.6–5.6)
Blood Urea Nitrogen (BUN), mmol/L	13.30 (7.43–20.80)
Creatinine, μmol/L	82.2 (53.1–113.6)
Sodium (Na), mmol/L	141.0 ± 5.4
Potassium (K), mmol/L	3.8 ± 0.5
Calcium (Ca), mmol/L	2.24 (1.81–2.39)
Lactate, mmol/L	1.6 (1.2–2.4)
Prothrombin time (PT), s	15.6 ± 2.4
Activated partial thromboplastin time (APTT), s	42.2 (37.8–47.3)
C-Reactive Protein (CRP), mg/L	84.45 (46.38–177.10)
Procalcitonin (PCT), ng/mL	1.40 (0.37–3.83)
Interleukin-6 (IL-6), pg/mL	87.61 (48.45–262.63)
Post-treatment parameters with eravacycline	
Vital signs	
Temperature, °C	36.9 (36.7–37.3)
Mean arterial pressure (MAP), mmHg	87 ± 11
Respiratory rate, breaths/min	20 (18–21.75)
Heart rate, beats/min	101 ± 20
Laboratory results	
White blood cell counts, × 10^9/L	9.3 (5.8–12.4)

(*Continued*)

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Table 3 (Continued).

Eravacycline Treatment	Overall (n = 24)
Neutrophil cell counts, × 10^9/L	7.56 (4.75–11.30)
Red blood cell counts, × 10^{12}/L	2.36 ± 0.51
Hemoglobin, g/L	76 ± 16
Platelet counts, × 10^9/L	123 (57–265)
ALT, U/L	19.5 (10–53)
AST, U/L	24 (16.25–49.75)
Total protein, g/L	56.6 ± 7.3
Albumin, g/L	37.6 ±5.7
Total bilirubin (TBIL), μmol/L	15.6 (10.9–24.2)
Direct bilirubin (DBIL), μmol/L	4.3 (3.1–6.6)
Blood Urea Nitrogen (BUN), mmol/L	10.79 (7.15–20.05)
Creatinine, μmol/L	53.5 (50–121)
Sodium (Na), mmol/L	139.0 (135.6–142.0)
Potassium (K), mmol/L	4.0 ± 0.6
Calcium (Ca), mmol/L	2.14 (1.21–2.33)
Lactate, mmol/L	1.8 (1.2–2.8)
Prothrombin time (PT), s	15.7 (15.0–18.3)
Activated partial thromboplastin time (APTT), s	39.4 (36.2–55.3)
C-Reactive Protein (CRP), mg/L	45.7 (10.10–87.33)
Procalcitonin (PCT), ng/mL	0.33 (0.12–1.90)
Interleukin-6 (IL-6), pg/mL	37.49 (20.04–150.05)

eravacycline-based antimicrobial therapy, these recipients were administered a variety of antibiotics, including cefoperazone-sulbactam, polymyxins, carbapenems, tigecycline, and minocycline.

The changes of various parameters before and after the treatment of eravacycline were presented in the Table 3. Prior to treatment, patients exhibited a slightly elevated heart rate, with an average of 106 beats per minute. The median counts of white blood cell and neutrophil cell exceeded the upper limit of the normal range. The average values of red blood cell and hemoglobin were below the normal range, as was the platelet count. The median blood urea nitrogen (BUN) and the average prothrombin time (PT) were both higher than the normal range. Inflammatory markers, including c-reactive protein (CRP), procalcitonin (PCT), and interleukin-6 (IL-6), had median values above the normal range. The analysis of eravacycline post-treatment revealed that the median white blood cell count fell within the normal range, while the median neutrophil count was close to the upper limit of normal. The average values of red blood cell and hemoglobin remained below the normal range, similar to pre-treatment levels. The median platelet count returned to within the normal range. Although the median BUN remained elevated compared to the normal range, it showed a decrease relative to baseline levels. The average PT remained abnormal, similar to pre-treatment values. The median values of CRP and IL-6 were mildly elevated, while the median PCT value was within the laboratory reference range. Overall, these inflammatory markers showed a decrease in their median levels post-treatment compared to baseline.

Table 4 The Outcomes of Eravacycline Treatment for CRAB Infections in Lung Transplant Recipients

Outcomes	Overall (n = 24)
14-day survival rate	24 (100.0%)
28-day survival rate	20 (83.3%)
Clinical failure rate	9 (37.5%)
Length of ICU stay, days	12.50 (6.00–20.75)
Length of hospital stay, days	55.08 ± 23.34

The outcomes of this study were illustrated in the Table 4. Among the 24 patients, the 14-day survival rate was 100%, but 4 patients died within 28 days after transplantation. Two recipients died from severe septic shock, another from a cerebrovascular accident, and the fourth succumbed to cardiogenic shock after experiencing cardiac and respiratory arrest event. Among these transplant recipients, 9 patients (37.5%) experienced clinical failure after treatment. The median length of ICU stay for all patients was 12.5 days (IQR, 6–20.75), with an average overall hospitalization length of 55.08 ± 23.34 days.

Details of The Comparison Between Patients with and without Clinical Failure

Table 5 presented a comparison of clinical characteristics between patients those who experienced clinical failure and those who did not following treatment with eravacycline. Statistical differences were observed in variables such as age, interstitial lung disease, septic shock, CRRT, and ICU length of stay. Compared to the group without clinical failure, patients who experienced clinical failure were older, had a higher proportion of interstitial lung disease, a higher incidence of septic shock, a greater proportion of CRRT treatment, and longer ICU stays. Regarding baseline parameters prior to eravacycline treatment, no significant differences were observed except for PT. After comparing post-treatment

Table 5 The Comparison Between Clinical Failure and Resolution Cases Following Eravacycline Therapy

Variables	Clinical Failure		P value
	Yes (n = 9)	No (n=15)	
Age, years	64.44 ± 9.84	49.20 ± 17.94	0.014
Native pulmonary disease			
Interstitial lung disease	7 (77.8%)	4 (26.7%)	0.033
Perioperative intensive care			
Continuous renal replacement treatment	6 (66.7%)	3 (20.0%)	0.036
Septic shock	5 (55.6%)	1 (6.7%)	0.015
Length of ICU stay, days	21 (16–64)	8 (5–17)	0.048
Pre-treatment parameters with ERA			
Laboratory results			
Prothrombin time (PT), s	16.3 (15.7–18.3)	14 (13.2–15.9)	0.020
Post-treatment parameters with ERA			

(*Continued*)

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Table 5 (Continued).

Variables	Clinical Failure		P value
	Yes (n = 9)	No (n=15)	
Vital signs			
Mean arterial pressure (MAP), mmHg	81 ± 7	91 ± 11	0.030
Heart rate, beats/min	114 (104–123)	88 (80–105)	0.030
Laboratory results			
ALT, U/L	46 (18–74)	11 (8–27)	0.021
AST, U/L	53 (18.5–114.5)	19 (14–32)	0.025
Total protein, g/L	52.1 ± 5.8	59.3 ± 6.9	0.015
Albumin, g/L	34.1 ± 4.9	39.7 ± 5.3	0.017
Prothrombin time, s	18.8 (16.5–19.9)	15.4 (14.0–15.8)	<0.001
Activated partial thromboplastin time (APTT), s	50.9 (39.8–75.1)	37.3 (33.6–46.2)	0.045
C-Reactive Protein (CRP), mg/L	91.9 (28.0–132.8)	36.4 (4.9–55.0)	0.025
Procalcitonin (PCT), ng/mL	2.12 (0.95–3.83)	0.16 (0.08–0.42)	0.003

Abbreviation: ERA, eravacycline.

vital signs and laboratory results, several variables showed statistical differences, including mean arterial pressure (MAP), heart rate, ALT, AST, total protein, albumin, PT, activated partial thromboplastin time (APTT), CRP, and PCT. Those who experienced clinical failure had lower MAP, an accelerated heart rate, elevated liver enzyme levels (ALT, AST), lower protein levels (total protein, albumin), prolonged PT and APTT, and increased levels of inflammatory markers (CRP, PCT).

Discussion

To the best of our knowledge, this observational study was the first to assess the efficacy of eravacycline against CRAB infections in lung transplant recipients. Our findings reported 14-day and 28-day survival rates of 100% and 83.3%, respectively, along with a clinical failure rate of 37.5% following treatment. This real-world study highlighted the use of eravacycline in lung transplant recipients with pulmonary infections, providing valuable evidence and clinical experience for its off-label use.

The global resistance rate of *Acinetobacter baumannii* clinical isolates continues to rise, particularly in regions such as Asia, Europe, and Latin America, where the proportion of CRAB isolates has exceeded 60%.[27] Even more concerning is the increasing resistance of CRAB isolates to critical antibiotics, such as ampicillin-sulbactam and colistin, as reported in studies worldwide.[28,29] This underscores the urgent need for the development of novel antibiotics and effective treatment strategies. Eravacycline, a novel fluorinated tetracycline antibiotic, has shown promising in vitro activity against CRAB. In vitro studies report that eravacycline's antimicrobial potency is 2–4 times greater than tigecycline, highlighting its superior overall efficacy. Moreover, eravacycline offers additional advantages, including higher concentrations in both serum and tissues (especially in the lungs) and improved tolerability.[30,31] Undoubtedly, novel antimicrobial agents like eravacycline represent a powerful weapon in the fight against CRAB infections.

In recent years, several randomized controlled trials (RCTs) and retrospective studies have been conducted to evaluate the effectiveness of eravacycline as a novel antibacterial option. According to the Phase II, Phase III clinical trials and real-world studies reported, eravacycline has demonstrated favorable efficacy, safety and well tolerance in clinical

practice. A phase II randomized, double-blind study aimed to evaluate the efficacy and safety of two doses of eravacycline compared with ertapenem in adult patients with community-acquired intra-abdominal infections.[18] The results showed comparable efficacy in each group, with eravacycline exhibiting good tolerability. A phase III multicenter randomized controlled trial (IGNITE 1) conducted by Solomkin et al demonstrated that eravacycline was non-inferior to ertapenem in adult hospitalized patients with cIAI, with good tolerability.[19] Subsequently, another RCT (IGNITE 4), also led by Solomkin et al, showed that eravacycline was non-inferior to meropenem in the treatment of adult patients with cIAI, including those caused by MDR pathogens, with a relatively low incidence of adverse reactions.[20] A subsequent pooled analysis combining two phase III RCTs explored the efficacy and tolerability of eravacycline in patients with cIAI and concomitant bacteremia.[32] The analysis revealed that eravacycline showed similar clinical outcomes and microbiological eradication rates to carbapenem antibiotics in patients with cIAI and related secondary bacteremia. Among patients in the microbiologic-intent-to-treat (micro-ITT) population with bacteremia at baseline, the pooled clinical response rate at the test-of-cure (TOC) follow-up point was 28/32 (87.5%) for eravacycline, compared to 24/31 (77.0%) for carbapenem, highlighting the potential of eravacycline in the treatment of bloodstream infections.

Furthermore, a real-world retrospective observational study assessed the efficacy and safety of eravacycline in critically ill patients with a variety of infections, including intra-abdominal infections, pneumonia, diabetic foot infections, and other infections.[33] It enrolled 50 patients, nearly half of whom had two or more pathogens isolated. In these patients, eravacycline showed a clinical efficacy of 94% in treating various infections, including those caused by MDR bacteria, along with good tolerability. This study provided insights into the real-world application and safety of eravacycline in patients with diverse infections and complex comorbidities. Another earlier multicenter, retrospective observational study included 35 infected patients, with the most common sources of infection being intra-abdominal (34%), followed by respiratory (29%), bone/joint (14%), and skin/soft tissue (9%).[34] Isolated pathogens included *Klebsiella pneumoniae, Enterococcus faecium, Acinetobacter baumannii*, and *Escherichia coli*. The study reported a 30-day survival rate of 74%, a 30-day relapse-free rate of 91%, and 57% of patients had resolution of infection signs and symptoms, while also demonstrating good tolerability. Additionally, the study noted that most infections in the cohort exceeded the FDA-approved indications for cIAI. Undoubtedly, these evidences underscore the potential of eravacycline as a promising treatment for various complex infections, including those involving MDR pathogens, and its favorable safety profile across different patient populations.

Due to the significant antibacterial advantages of eravacycline,[6] multiple real-world studies have explored its expanded use, along with the growing body of real-world evidences providing its off-label clinical applications. A multicenter observational study by Hobbs et al retrospectively evaluated the efficacy of eravacycline in 66 patients.[35] Notably, the majority of the patients (68.2%) received treatment beyond the labeled indications for eravacycline, including 34.8% with pulmonary infections and 28.8% with skin/soft tissue infections. The identified Gram-negative pathogens in these cases showed 50% resistant to carbapenems in vitro, while Gram-positive pathogens exhibited 48% resistant to vancomycin in vitro. A clinical improvement was observed in 95.5% of the patients, with 86.4% achieving complete resolution of the infection. This suggested that eravacycline possessed a broad spectrum of activity with favorable safety and tolerability profiles.

In another real-world multicenter cohort study, 46 patients received eravacycline treatment for *Acinetobacter baumannii* infections, with 65% of cases being CRAB.[21] The main infection site was the lungs (58.3%), and the study accessed the 30-day mortality rate (23.9%) and adverse event rate (2.1%). While the study reported positive clinical outcomes with eravacycline treatment, it also highlighted the uncertainty regarding its clinical benefits in solid organ and bone marrow transplant recipients. Our study addressed this gap by providing clinical evidence for the use of eravacycline in treating CRAB infections in lung transplant recipients. Due to the immunocompromised state of this population, 62.5% of patients achieved clinical resolution in our cohort, which was similar to the clinical resolution rate observed in a recent retrospective case series.[36] This case series also analyzed eravacycline in combination therapy for ventilator-associated pneumonia due to CRAB in 24 patients with COVID-19. The results indicated that 71% of patients achieved both clinical resolution and microbiological eradication. However, the study's limitations were acknowledged, particularly the difficulty in controlling for confounding variables, such as distinguishing between colonization and infection in CRAB sputum cultures, polymicrobial infections in most patients and severe COVID-19 infections. In our

study, the high risk of infection due to immunosuppression status also led to polymicrobial infections in some cases, although other potential pathogens were not explicitly listed, which represents a limitation of our study.

Other limitations should also be considered. First, it was a single-center, retrospective study with a relatively small sample size, which inherently limited generalizability compared to larger retrospective studies or RCTs. This might be partly due to the relatively limited transplant population and the relatively recent availability of eravacycline in our region, coupled with its higher cost. Second, this study was a non-comparative observational study without a control group, along with potential confounding factors. As such, definitive conclusions regarding the comparative efficacy of eravacycline cannot be drawn. Furthermore, we were unable to obtain the MIC values for all isolated strains of eravacycline, which was another limitation. Given these constraints, large-scale RCTs with larger sample sizes were required to further validate the efficacy of eravacycline in the treatment of off-label CRAB infections. Although eravacycline shows promise, the development of additional therapeutic options remains vital. Novel agents under investigation, as well as combinations targeting resistance mechanisms directly, will be crucial in overcoming evolving CRAB phenotypes.

In our study, we observed significant differences in several characteristics between the clinical failure group and the clinical resolution group. Our analysis indicated that the clinical failure group was characterized by older patients, a higher incidence of septic shock, a greater proportion of patients receiving CRRT, and longer ICU stays. A prospective observational study conducted by Dalfino et al,[37] which focused on patients with ventilator-associated pneumonia caused by CRAB, compared those with clinical resolution to those with clinical failure. It similarly found that patients with clinical failure were older, had a higher comorbidity burden, more severe clinical conditions, and higher rates of immunosuppression. Previous research had consistently underscored the relationship between age and mortality risk, with a significant positive correlation observed between age and both early and late mortality.[38] Specifically, patients over 65 years of age with *Acinetobacter baumannii* infection exhibited a higher mortality rate compared to those aged 65 or younger.[38] Septic shock was a well-established factor associated with poor prognosis. In an observational cohort study evaluating treatment regimens for CRAB ventilator-associated pneumonia, multivariable logistic regression analysis, adjusted for propensity scores, revealed that septic shock was significantly associated with increased mortality.[39] Similar findings had been reported in other studies.[40–43] Additionally, a prospective observational study conducted in multiple hospitals on CRAB bloodstream infections revealed that CRRT was independently associated with an increased risk of septic shock through multivariable analysis.[44] Therefore, it was not surprising that patients in the clinical failure group in our study were older, had a higher proportion requiring CRRT, and had a higher likelihood of developing septic shock. These factors collectively contributed to a higher severity of infection, which presented significant challenges for antimicrobial therapy, limited treatment efficacy, and ultimately explained the prolonged ICU stays.

Conclusion

This real-world observational study represented the first to describe the clinical application of eravacycline in treating CRAB infections in lung transplant recipients, providing valuable evidence and clinical experience for the off-label application of eravacycline. Further large-scale, prospective studies or randomized controlled trials are warranted to more comprehensively evaluate the efficacy of eravacycline.

Abbreviations

CRAB, Carbapenem-resistant *Acinetobacter baumannii*; AMR, Antimicrobial Resistance; WHO, World Health Organization; MDR, multidrug resistance; XDR, extensively drug-resistant; CRE, Carbapenem-resistant *Enterobacteriaceae*; cIAI, complicated intra-abdominal infections; ECMO, extracorporeal membrane oxygenation; CRRT, continuous renal replacement therapy; KDIGO, Kidney Disease Improving Global Outcomes; IQR, interquartile range; BUN, blood urea nitrogen; PT, prothrombin time; CRP, C-reactive protein; PCT, Procalcitonin; IL-6, Interleukin-6; MAP, mean arterial pressure; APTT, Activated partial thromboplastin time; RCTs, randomized controlled trials; micro-ITT, microbiologic-intent-to-treat; TOC, test-of-cure.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Statement

This study was approved by the Research Ethics Committee of Second Affiliated Hospital of Zhejiang University School of Medicine (approval number: 2025-0212) and was conducted in accordance with the Declaration of Helsinki. The organ donation and transplantation procedures adhered to the Declaration of Istanbul. None of the donor lungs for lung transplant recipients at our hospital were obtained from prisoners, and all organ donations were sourced exclusively through voluntary organ donation. All patient data were anonymized and maintained with strict confidentiality.

Author Contributions

All authors contributed to the work reported, including the conception, study design, execution, data collection, analysis and interpretation; They were involved in drafting, revising or critically reviewing the manuscript, and provided final approval of the version for publication. They have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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