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The efficacy and safety of eravacycline in the treatment of patients with pneumonia in respiratory departments: A real-world multicenter retrospective study

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ABSTRACT

Introduction: Eravacycline (ERV), a novel fluorocycline antibiotic, demonstrates broad-spectrum activity against multidrug-resistant (MDR) pathogens. This multicenter retrospective study evaluates the real-world clinical effectiveness of ERV in treating various infections of the patients hospitalized in the respiratory departments.

Methods: We analyzed 113 adult patients treated with ERV from respiratory departments in China, examining antimicrobial susceptibility profiles and serial laboratory parameters during therapy. Microbiological and clinical outcomes were systematically evaluated at treatment completion and 30-day follow-up. Subgroup analyses focused on *Acinetobacter baumannii* and *Klebsiella pneumoniae* infections.

Results: ERV exhibited 87.6% clinical efficacy and 85.8% microbiological eradication rate, accompanied by an 85.0% 30-day survival rate. The antibiotic maintained robust activity against MDR pathogens, particularly *A. baumannii* ($n = 51$) and *K. pneumoniae* ($n = 27$). Adverse events occurred in only 1.8% (2/113) of cases. Clinical outcomes showed no statistically significant differences between monotherapy ($n = 70$) and combination regimens ($n = 43$).

Conclusion: This real-world evidence confirms ERV as an effective and well-tolerated therapeutic option for managing patients in the respiratory departments, particularly those caused by MDR Gram-negative pathogens. The comparable efficacy of monotherapy and combination approaches warrants further investigation.

1. Background

Antimicrobial resistance (AMR) represents a significant global health threat, and the rising prevalence of AMR has severely limited therapeutic options, leading to increased morbidity, mortality, and healthcare costs. According to a previous systematic analysis, there were an estimated 4.95 million deaths associated with bacterial AMR in 2019, including 1.27 million deaths attributable to bacterial AMR [1]. In particular, resistance to Gram-negative pathogens, including carbapenem-resistant Enterobacteriaceae and carbapenem-resistant *Acinetobacter baumannii*, presents an urgent public health threat. Therefore, the ongoing development of novel antimicrobial agents with an expanded spectrum of activity is critical to address both current clinical challenges and the anticipated evolution of resistance mechanisms [2,3].

Eravacycline (ERV) is a novel fluorocycline antibiotic designed to overcome resistance to common tetracycline-specific efflux and ribosomal protection mechanisms [4], and it demonstrates robust activity against a wide range of multidrug-resistant (MDR) pathogens, such as methicillin-resistant *Staphylococcus aureus* strains, vancomycin-resistant *Enterococcus* faecium and *Enterococcus faecalis*, extended spectrum blactamase-roducing Enterobacteriaceae, AmpC-producing Enterobacteriaceae, and carbapenem-resistant strains, including carbapenemase-producing Enterobacteriaceae and *A. baumannii* [5,6]. In 2018, ERV received approval from the U.S. Food and Drug Administration (FDA) for the treatment

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of complicated intra-abdominal infections (cIAIs) in adult patients aged 18 years and older [6].

Previous studies have evaluated the efficacy and safety of ERV in the treatment of cIAIs [7,8] and the antibacterial activity of ERV in vitro was evaluated [9,10]. In recent years, numerous studies have also assessed the clinical outcomes of ERV in various therapeutic contexts [11–13]. In the respiratory departments, management of infections continues to depend on older antibiotics or combinations associated with notable toxicity risks, such as colistin or aminoglycosides. While in vitro studies suggest ERV's efficacy against common respiratory pathogens, such as *K. pneumonia* and *A. baumannii*, clinical data in this setting are sparse. Retrospective analyses are critical to evaluate real-world effectiveness and safety, particularly in vulnerable populations with comorbidities or prior antibiotic exposure. This study aims to address this gap by assessing ERV's role in the respiratory departments, focusing on clinical outcomes (e.g., resolution of symptoms, microbiological eradication) and safety profiles. Findings may inform optimized antibiotic stewardship and provide evidence for expanding ERV's therapeutic indications in respiratory care.

2. Methods

2.1. Population and sample selection

Data in this study were obtained from the project conducted by the Expert Committee on Drug Clinical Application and Drug Resistance Evaluation under the National Health Commission of China, which is a multicenter, observational study designed to collect clinical data on Chinese patients who have been treated with ERV in routine clinical practice. The participants' inclusion criteria were as follows: (1) critically ill patients aged 18 years or older, (2) administration of ERV for a minimum of three days for the treatment of infections at various sites, (3) admission to the respiratory departments, and (4) a follow-up period of 30 days. The exclusion criteria included: (1) individuals younger than 18 years, (2) hospital stays longer than 100 days.

The pneumonia diagnosis was made according to the Infectious Diseases Society of America (IDSA) guidelines for Hospital-Acquired Pneumonia (HAP) and Ventilator-Associated Pneumonia (VAP) [14,15]. Cases were rigorously categorized as follows: (1) VAP: Pneumonia occurring ≥48 h after endotracheal intubation. (2) HAP: Pneumonia occurring ≥48 h after hospital admission in non-intubated patients. Diagnosis and classification were confirmed by infectious disease or pulmonary specialists based on the concurrent presence of the following criteria:

(1) Radiographic Evidence: New or progressive pulmonary infiltrate confirmed by chest radiography or computed tomography (CT).
(2) At least two of the following clinical manifestations: A. Fever (> 38.0 °C) or hypothermia (< 36.0 °C), B. Leukocytosis (> 12,000 cells/mm^3), leukopenia (< 4000 cells/mm^3), or > 10% immature band forms. C. Purulent tracheobronchial secretions or documented change in sputum characteristics.
(3) Microbiological Confirmation: Evidence substantiating infection beyond colonization, utilizing one of these approaches: A. Pathogen isolation at or above established thresholds, e.g., Bronchoalveolar Lavage (BAL) ≥ 10^4 CFU/mL. B. Pathogen growth in sputum supplemented by ≥1 ancillary indicator: Significant Gram stain findings (> 25 neutrophils per low-power field on BAL cytology); Inflammatory markers: C-reactive protein (CRP) or procalcitonin (PCT) elevated.

2.2. Data collection

The following patient characteristics were systematically collected: demographics, underlying conditions, immunosuppressive treatment regimens, recent surgical history, mechanical ventilation status, sequential organ failure assessment (SOFA) scores, and laboratory test results (white blood cell (WBC) count, neutrophil count, CRP, and PCT levels) obtained prior to treatment, on day three, and at the end of treatment. Additionally, clinical outcomes at the end of treatment and at day 30 were recorded. The effectiveness of ERV treatment is assessed based on a three-level objective evaluation: recovery, significant improvement, and ineffectiveness. Recovery and significant improvement are defined as effective. Recovery is defined as the disappearance of symptoms and signs of infection, including the normalization of experimental indicators and temperature at the end of ERV treatment, along with the eradication or presumed eradication of the pathogen. Significant improvement refers to a marked improvement in symptoms, signs, and supporting test results related to the infection, although at least one of these indicators remains abnormal. Ineffectiveness is defined as the absence of improvement or a worsening of symptoms and signs.

Microbiological characteristics included: identification of the causative pathogen(s), antimicrobial susceptibility testing (AST) using broth microdilution and/or disk diffusion methods, and microbiological outcomes at the end of treatment. Microbiological efficacy is categorized as either effective or ineffective. Effective includes pathogen clearance, presumed clearance, and bacterial alterations, while the ineffective category includes persistent presence of the pathogen and presumed non-clearance. Furthermore, characteristics of ERV therapy were documented, including the administered dose, duration of intravenous infusion, and adverse effects. According to the ChinaCAST guidelines, susceptibility to ERV is defined as a minimum inhibitory concentration (MIC) ≤1 mg/L by broth microdilution or a zone of inhibition ≥15 mm by disk diffusion.

2.3. Statistical analyses

GraphPad Prism 8 was used for statistical analysis. Measurement data were presented as mean ± standard deviation, with *t*-tests or analysis of variance (ANOVA) used for comparing group means. Categorical data were expressed as percentages and analyzed using the χ^2 test. A p-value of less than 0.05 indicated statistical significance.

3. Results

3.1. Patients' characteristics

A total of 113 patients, originating from 21 provinces across China, received ERV treatment in the respiratory departments between September 2023 and September 2024. The proportion of males in the study population is 67.3% (76/113). The mean age was 66.53±17.97 years, with a wide age distribution suggesting broad age representation within the cohort. Chronic disease profiling revealed pulmonary disorders as the most prevalent comorbidity (70.8%, 80/113), followed by kidney disease (23.0%, 26/113) and central nervous system disorders (20.4%, 23/113). Additional comorbidities included solid tumors (8.0%, 9/113) and hematological diseases (8.8%, 10/113) (Table 1).

Regarding clinical assessments, a significant number of participants have undergone various medical interventions. For example, 45.1% (51/113) have received mechanical ventilation, 39.8% (45/113) have had tracheal cannula insertion, and 41.6% (47/113) have had gastric tube insertion. The SOFA score averaged 4.86 ± 4.70, and the time of ERV application was administered for a mean duration of 9.70 ± 4.74 days, while the average hospital stays extended to 32.40 ± 30.04 days (Table 1).

Table 1
Demographics and baseline characteristics of the study population (n = 113).

Characteristic	n (%)
Male	76 (67.3)
Age (years)*	66.53 ± 17.97
Chronic disease	
Pulmonary disease	80 (70.8)
Solid Tumor	9 (8.0)
Hematological Disease	10 (8.8)
Kidney Disease	26 (23.0)
Central nervous system disease	23 (20.4)
CVD	56 (49.6)
DM	37 (32.7)
AIDS	4 (3.5)
Autoimmune rheumatic diseases	8 (7.1)
Transplantation of organs	5 (4.4)
Granulocytopenia	8 (7.1)
Other underlying diseases	34 (30.1)
Mechanical ventilation	51 (45.1)
Recent surgery	6 (5.3)
Arterial cannula	14 (12.4)
Central vein catheter	38 (33.6)
Tracheal cannula	45 (39.8)
Tracheotomy	27 (23.9)
Indwelling urine catheter	41 (36.3)
Gastric tube insertion	47 (41.6)
Other catheter	6 (5.3)
corticosteroid/immunosuppressant use (long-term)	15 (13.3)
History of antimicrobial	60 (53.1)
SOFA*	4.86 ± 4.70
Time of ERV application(d)*	9.70 ± 4.74
Length of hospital stay(d)*	32.40 ± 30.04

* (Mean ± SD), CVD: cardiovascular disease; DM: Diabetes mellitus; AIDS: acquired immunodeficiency syndrome; SOFA: sequential organ failure assessment; ERV: eravacycline.

3.2. Infections in patients and the antimicrobial susceptibility of isolates

Among the 113 cases, pneumonia is the most prevalent infection type, accounting for 86.7% (98/113). Among these 98 pneumonia patients, 54 were classified as HAP, and 44 were classified as VAP (Table 2).

Of the 113 patients, 92 provided microbiological examination results, with 51 cases identified as *A. baumannii* (48 single infection cases) and 27 cases infected with *K. pneumoniae* (26 single infection cases) (Table 2). Both pathogens were primarily isolated from sputum (*A. baumannii*: 57.8%, *K. pneumoniae*: 57.7%) and BAL (*A. baumannii*: 40%, *K. pneumoniae*: 38.5%), followed by ascites (*A. baumannii*: 2.2%, *K. pneumoniae*: 3.8%). Among the 54 HAP cases, microbiological results were available for 33 patients: 23 with *A. baumannii* and 10 with *K. pneumoniae* infections. Similarly, among the 44 VAP cases, 33 had microbiological results available: 20 with *A. baumannii* and 13 with *K. pneumoniae* infections.

According to the information uploaded by participating hospitals, the antimicrobial susceptibility of ERV, tigecycline, imipenem, meropenem and colistin were analyzed. The data showed that ERV showed high efficacy against both *A. baumannii* and *K. pneumoniae*. A total of 89.3% (25/28) of *A. baumannii* isolates were susceptible to ERV, and 100% (11/11) of *K. pneumoniae* isolates were susceptible to ERV. *A. baumannii* also demonstrated high susceptibility to tigecycline and colistin, with 91.9% (34/37) and 96.6% (28/29) of strains, respectively, exhibiting susceptibility. However, the pathogen displayed significant resistance to imipenem and meropenem, with only 4% (1/25) and 12% (3/25) of the strains, respectively, being susceptible to these antibiotics. The susceptibility of *K. pneumoniae* to tigecycline and colistin was lower than that of *A. baumannii*, with 76.5% (13/17, P = 0.189) and 55.6% (5/9, P = 0.008) of strains, respectively, showing susceptibility. However, *K. pneumoniae* exhibited higher susceptibility to imipenem and meropenem compared to *A. baumannii*, with 41.2% (7/17, P = 0.004) and 75% (4/16, P = 0.401) of strains, respectively, being susceptible to these antibiotics (Table 3).

Table 3
Antimicrobial susceptibility of clinical isolates.

Antimicrobial susceptibility	*A. baumannii*	*K. pneumoniae*	*P*
Eravacycline	89.3% (25/28)	100% (11/11)	0.545
Imipenem	4% (1/25)	41.2% (7/17)	0.004
Meropenem	12% (3/25)	75% (4/16)	0.401
Tigecycline	91.9% (34/37)	76.5% (13/17)	0.189
Colistin	96.6% (28/29)	55.6% (5/9)	0.008

3.3. Clinical and microbiological outcomes

In this study, 95.6% (108/113) of patients followed a dose of 1 mg/kg/12 h and the average treatment duration was 9.7 days. Following a three-day course of intravenous ERV administration, there was a statistically significant reduction in WBC, neutrophil count, CRP, and PCT levels compared to pre-treatment values (P < 0.001). Additionally, the SOFA score demonstrated a significant decrease post-treatment (P < 0.05) (Supplementary Table 1).

In terms of clinical effectiveness at the end of the treatment (The day of discontinuing ERV), 99 (87.6%) patients had an effective clinical outcome, among whom 20 cases recovered and 79 cases showed significant improvement. Among 98 patients with pneumonia, 88 achieved effective outcomes, including 51 cases of HAP and 37 cases of VAP. At the end of ERV therapy, the effective rates for HAP and VAP were 94.4% and 84.1%, respectively. 46 (90.2%) *A. baumannii*-infected patients and 22 (81.5%) *K. pneumoniae*-infected patients had an effective clinical outcome. Only five patients (4.4%) had an ineffective clinical outcome. Mortality rates were also presented, with nine patients (8.0%) dying during this period, two (3.9%) from the *A. baumannii* group and five (18.5%) from the *K. pneumoniae* group. There was one death in the HAP group and five deaths in the VAP group, with no significant difference in each data. The clinical outcomes at day 30 are similar to those at the end of ERV treatment (Table 4). Among the 113 patients, for the microbiological effectiveness, 97 patients (85.8%) had an effective outcome, with 44 (86.3%) of those infected with *A. baumannii* and 22 (81.5%) of those infected with *K. pneumoniae*. The clearance rate reached 40.7% (46/113) of all patients, and the presumed clearance rate was 39.8% (45/113).

As for patients with pneumonia, both clinical efficacy and microbiological efficacy reached 89.8% at the end of ERV treatment (Table 4). Of the 113 patients, only two reported adverse reactions,

Table 2
Clinical diagnosis of infection types and pathogens.

Infection type (n = 113)	n (%)	Pathogen of the infection n (%)	
		A. baumannii (n = 51)	*K. pneumoniae* (n = 27)
Pneumonia	98 (86.7)	43 (84.3)	23 (85.2)
HAP	54 (55.1)	23 (53.5)	10 (43.5)
VAP	44 (44.9)	20 (46.5)	13 (56.5)
Others	15 (13.3)	8 (15.7)	4 (14.8)

Table 4
Microbiological and clinical outcomes of patients infected with different strains.

	Total patients (n = 113)	Patients with pneumonia (n = 98)	HAP Patients (n = 54)	VAP Patients (n = 44)	P[a]	Patients infected with *A. baumannii* (n = 51)	Patients infected with *K. pneumoniae* (n = 27)	P[b]
Microbiological outcomes at end of ERV treatment					0.107			0.742
Effective	97 (85.8%)	88 (89.8%)	51 (94.4%)	37 (84.1%)		44 (86.3%)	22 (81.5%)	
Clearance	46 (40.7%)	42 (47.7%)	24 (47.1%)	18 (48.6%)		19 (43.2%)	12 (54.5%)	
Presumed clearance	45 (39.8%)	40 (45.5%)	25 (49.0%)	15 (40.6%)		21 (47.7%)	9 (41.0%)	
Bacterial alterations	6 (5.3%)	6 (6.8%)	2 (3.9%)	4 (10.8%)		4 (9.1%)	1 (4.5%)	
Ineffective	16 (14.2%)	10 (10.2%)	3 (5.6%)	7 (15.9%)		7 (13.7%)	5 (18.5%)	
Clinical outcomes at end of ERV treatment					0.149			0.087
Effective	99 (87.6%)	88 (89.8%)	51 (94.4%)	37 (84.1%)		46 (90.2%)	22 (81.5%)	
Recovery	20 (20.2%)	20 (22.7%)	15 (29.4%)	5 (13.5%)		6 (13.0%)	5 (22.7%)	
Significant improvement	79 (79.8%)	68 (77.3%)	36 (70.6%)	32 (86.5%)		40 (87.0%)	17 (77.3%)	
Ineffective	5 (4.4%)	4 (4.1%)	2 (3.7%)	2 (4.5%)		3 (5.9%)	0 (0%)	
Mortality	9 (8.0%)	6 (6.1%)	1 (1.9%)	5 (11.4%)		2 (3.9%)	5 (18.5%)	
Clinical outcomes at day 30					0.052			0.151
Effective	96 (85.0%)	85 (86.7%)	50 (92.6%)	35 (79.5%)		46 (90.2%)	21 (77.8%)	
Recovery	43 (44.8%)	40 (47.1%)	19 (38.0%)	21 (60.0%)		18 (39.1%)	13 (61.9%)	
Significant improvement	53 (55.2%)	45 (52.9%)	31 (62.0%)	14 (40.0%)		28 (60.9%)	8 (38.1%)	
Ineffective	4 (3.5%)	3 (3.1%)	2 (3.7%)	1 (2.3%)		1 (2.0%)	0 (0%)	
Mortality	13 (11.5%)	10 (10.2%)	2 (3.7%)	8 (18.2%)		4 (7.8%)	6 (22.2%)	

[a] Patients in HAP and VAP groups.
[b] Patients infected with *A. baumannii* and *K. pneumoniae* groups.

namely gastrointestinal reactions (nausea, vomiting) and elevated liver enzymes.

3.4. Comparison of therapeutic outcomes of single-pathogen and mixed-pathogen infections

Among 92 patients with reported microbiological examination results, 87 cases (94.6%) exhibited single-pathogen infections while 5 cases (5.4%) demonstrated mixed-pathogen infections. *A. baumannii* was identified as the most prevalent pathogen in single-pathogen infections, accounting for 55.2% of cases, followed by *K. pneumoniae* (29.9%), *E. coli* (2.3%), *Stenotrophomonas maltophilia* (1.1%), and *Enterococcus faecium* (1.1%). In five mixed-pathogen infection cases, the pathogens identified were *A. baumannii* and *Cyclospora* spp., *A. baumannii* and *K. pneumoniae, Elizabethkingia meningoseptica* and *Pseudomonas aeruginosa, A. baumannii* and *Burkholderia cepacian, A. baumannii* and *Chlamydia psittaci.*

At end of ERV treatment, the effective rate of the single-pathogen infection group reached 87.4%, and that of the mixed-pathogen infection group was 80%. The recovery rates of the two groups were 13.2% and 25% respectively. On the 30th day, the recovery rate of the single-pathogen infection group rose to 43.2%. At end of ERV treatment, the mortality rate of single-pathogen cases was 8.0%, while the value of mixed infections was 20.0%. The fatal case involved the mixed-pathogen infection with *A. baumannii* and *Chlamydia psittaci*. This patient was diagnosed with severe pneumonia, septic shock, type I respiratory failure, and sepsis. Microbiological outcomes revealed 87.4% effectiveness (76/87) in single-pathogen cases compared to 60.0% (3/5) in mixed infections. The laboratory test results also showed in Supplementary Table 2. The microbiological and clinical outcome differences, and laboratory test results did not reach statistical significance (Supplementary Table 2), likely influenced by the small mixed-infection cohort.

3.5. Comparison of therapeutic outcomes of ERV alone and combination therapy

For clinical outcomes at the end of ERV treatment, 64 patients (87.7%) in the combination therapy group and 35 (87.5%) in the monotherapy group had an effective outcome. The ineffectiveness rates were 6.8% (5/73) in the combination therapy group and 0% in the monotherapy group. By day 30, clinical efficacy rates remained stable in both groups (combination: 83.5%; monotherapy: 87.5%). At the end of treatment, efficacy rates of microbiological outcomes were comparable between combination therapy (86.3%) and monotherapy (85.0%), with corresponding inefficacy rates of 13.7% (10/73) versus 15.0% (6/40) (Supplementary Table 3).

The laboratory test results of the combination therapy and monotherapy groups were also analyzed. Except for the neutrophil count, the WBC count, neutrophil ratio, CRP level, PCT level, and SOFA score did not exhibit significant differences between the two groups (Supplementary Table 3).

4. Discussion

As a novel fluorocycline antibiotic, ERV was FDA-approved for treating cIAIs in adults. Given its robust activity against MDR pathogens, ERV demonstrates potential utility across broader infectious indications. However, no comprehensive international studies have evaluated ERV's efficacy in the hospitalized patients from respiratory departments. This real-world multicenter observational analysis included 113 patients from respiratory department receiving ERV. Among these 113 patients, 98 were classified as pneumonia patients, including 54 with HAP and 44 with VAP. The distribution of *A. baumannii* and *K. pneumoniae* infections among HAP and VAP patients was comparable: 23 *A. baumannii* and 10 *K. pneumoniae* in HAP patients, versus 20 *A. baumannii* and 13 *K. pneumoniae* in VAP patients. At the end of ERV treatment, microbiological effectiveness rates (94.4% vs 84.1%) and clinical effectiveness rates (94.4% vs 84.1%) were higher in HAP patients compared to VAP patients, though these differences were not statistically significant. Due to unavoidable limitations during data collection, however, we were unable to provide ventilated HAP-related data, which represents a minor gap in the present analysis of patient outcomes.

As a leading cause of nosocomial infections in modern healthcare systems, *A. baumannii* represents a significant therapeutic challenge due to its multidrug-resistant nature and invasive pathogenic characteristics [16]. Our findings revealed that clinical isolates of *A. baumannii* demonstrated resistance rates of 96% to imipenem and 88% to meropenem, while maintaining 89.3% sus-

ceptibility to ERV. This antimicrobial profile corresponded with favorable clinical outcomes, as evidenced by an 90.2% effectiveness rate in ERV-treated *A. baumannii* infections. The observed treatment failures in ERV therapy may be attributed to evolving resistance mechanisms, including potential heteroresistance development, despite current high susceptibility rates. For example, emerging reports document concerning resistance patterns: Chen et al. [17] identified ISAba1 insertions in *adeS* associated with ERV resistance, Li et al. [18] observed ERV heteroresistance in Chinese carbapenem-resistant *A. baumannii* strains, and Dutch investigators [19] reported hospital-acquired transmission of ERV-resistant *A. baumannii* carrying tet (x3), blaNDM-1, and blaOXA-97 resistance determinants. Carbapenem-resistant *K. pneumoniae* (CRKP) infections also pose a critical public health challenge due to their substantial mortality burden [20].

Notably, ERV demonstrates potent activity against carbapenem-resistant Gram-negative bacteria, particularly exhibiting efficacy against 61.3% of NDM-producing and 66.7% of VIM-producing CRKP strains [21]. Nevertheless, the emergence of ERV resistance in CRKP mediated by efflux pump overexpression has been clinically documented [22]. Despite partial resistance to imipenem, meropenem, tigecycline, and colistin observed in some *K. pneumoniae* strains, all tested isolates in this investigation demonstrated full susceptibility to ERV, correlating with favorable therapeutic outcomes: 81.5% microbiological effectiveness and 81.5% clinical efficacy rates were achieved. This discrepancy may stem from the restricted sample size ($n = 11$), which could potentially miss undetected ERV-resistant strains. Additionally, multiple clinical variables likely contribute to this therapeutic gap, including pharmacokinetic challenges such as differential tissue penetration efficiency and pharmacodynamic considerations involving host immunological status. The complexity of real-world clinical environments -encompassing polymicrobial infections, biofilm formation dynamics, and antibiotic stewardship variations-further complicates direct extrapolation from standardized antimicrobial susceptibility testing outcomes to bedside management.

This study demonstrated favorable therapeutic efficacy of ERV in retreatment of patients from respiratory departments, achieving an 87.6% clinical cure rate, 85.8% microbiological eradication rate, and 88.5% 30-day survival rate-notably surpassing the 74% survival rate reported by Alosaimy S [11]. Furthermore, ERV has demonstrated both safety and efficacy in the treatment of pulmonary infections in this study. The comparative analysis revealed comparable clinical efficacy between ERV monotherapy and combination regimens, with 87.7% (64/73) of combination therapy patients and 87.5% (35/40) of monotherapy patients achieving clinical success at treatment completion, followed by sustained efficacy through day 30 (combination: 83.5%; monotherapy: 87.5%). Microbiological outcomes paralleled these trends, demonstrating near-identical eradication rates (combination: 86.3%; monotherapy: 85.0%). Nevertheless, synergistic potential warrants further investigation [23,24]. Li et al. [25] identified ERV-polymyxin B combinations as the most effective against carbapenem-resistant *E. coli* and *K. pneumoniae* (≥30% synergy), whereas ERV-ceftazidime and ERV-imipenem combinations exhibited superior activity against carbapenem-resistant *A. baumannii* (≥50% synergy). Contrastingly, Yin et al. [26] observed in vitro synergism with ERV-imipenem combinations against select isolates, though this did not translate into improved survival outcomes in murine models of MDR *A. baumannii* infection compared to monotherapy.

Among 113 patients receiving treatment in this study, only two experienced adverse reactions, nausea and vomiting and elevated liver enzymes, aligning with findings from prior reports (1 of 46 patients had adverse reactions) [12]. Current evidence remains inconclusive regarding ERV's safety profile, with persistent discrepancies observed across clinical trials. Notably, a large-scale meta-analysis by Chen et al. demonstrated a statistically significant elevation in treatment-emergent adverse events with ERV compared to standard therapies (OR = 1.55, 95% CI = 1.21–1.99), highlighting the need for population-specific risk stratification in therapeutic decision-making [27].

In conclusion, ERV demonstrates promising clinical utility in respiratory departments, achieving notable clinical cure and microbiological eradication rates with favorable 30-day survival outcome. Its preserved activity against multidrug-resistant pathogens, including carbapenem-resistant *A. baumannii* and *K. pneumoniae*, positions it as a valuable therapeutic alternative in antimicrobial-resistant pneumonia management. While exhibiting an advantageous safety profile, emerging resistance patterns and inconsistent synergistic benefits with combination therapies underscore the need for judicious use and ongoing resistance surveillance. Due to the lack of corresponding data, we regretfully could not further differentiate ventilated HAP to provide more comprehensive insights alongside the HAP and VAP data presented. Addressing this gap is crucial for developing effective prevention and management strategies spanning the entire patient journey. Future studies should therefore prioritize optimization of dosing strategies, longitudinal monitoring of resistance evolution, and close tracking of ventilator usage patterns to sustain ERV's clinical efficacy in respiratory care.

Declaration of competing interest

The authors declare that they have no competing interests.

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Ethics approval

The current study was approved by the ethics committee of Peking Union Medical College Hospital (Protocol code I-23ZM0067, October 2023).

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jgar.2025.09.011.

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