INPLASY

Efficacy of Sulbactam-Durlobactam for Carbapenem-Resistant Acinetobacter baumannii Infections: A Systematic Review and Single-Arm Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 May 2026 and was last updated on 17 May 2026.

INTRODUCTION

Review question / Objective This study evaluated the efficacy of SUL-DUR for the treatment of CRAB infections through a meta-analysis. the PICOS framework is defined as follows:
Population (P): Adult patients (≥18 years) with microbiologically confirmed CRAB infection (including but not limited to pneumonia, bloodstream infection, central nervous system infection, skin and soft tissue infection, and intra-abdominal infection).
Intervention (I): Treatment with sulbactam-durlobactam (SUL-DUR) administered either as monotherapy or in combination with other antibiotics (e.g., carbapenems, polymyxins, tigecycline, cefiderocol), for a duration of at least 48 hours.
Comparator (C): Not applicable – this is a single-arm meta-analysis of studies where all patients received SUL-DUR (no active comparator or placebo group required).
Outcome (O):
Primary outcome: Overall survival (defined as survival to hospital discharge, 28-day survival, or clinical cure as reported by the original study).
Secondary outcome: Microbiological clearance (defined as negative follow-up culture from the primary infection site after treatment).
Study design (S): Prospective or retrospective case reports, case series (including those reported as meeting abstracts), and the published phase 3 randomized controlled trial (ATTACK trial). Reviews, editorials, in vitro studies, and studies without original clinical outcome data were excluded.

Condition being studied Carbapenem-resistant Acinetobacter baumannii (CRAB) is a Gram-negative opportunistic pathogen that primarily causes healthcare-associated infections, including ventilator-associated pneumonia, bloodstream infections, central nervous system infections, skin and soft tissue infections, and intra-abdominal infections. CRAB exhibits high levels of resistance to multiple antibiotic classes, including carbapenems, due to a variety of mechanisms such as production of OXA-type

carbapenemases, upregulation of efflux pumps, porin loss, and target site modifications. Infections caused by CRAB are associated with high morbidity and mortality (up to 40–60% in critically ill patients), and treatment options are extremely limited. The World Health Organization has listed CRAB as a priority 1 critical pathogen, highlighting the urgent need for new effective antibiotics. Sulbactam-durlobactam (SUL-DUR) is a novel β-lactam/β-lactamase inhibitor combination specifically developed to overcome CRAB resistance.

METHODS

Participant or population Adult patients (≥18 years) with microbiologically confirmed CRAB infection (including but not limited to pneumonia, bloodstream infection, central nervous system infection, skin and soft tissue infection, and intra-abdominal infection).

Intervention Treatment with sulbactam-durlobactam (SUL-DUR) administered either as monotherapy or in combination with other antibiotics (e.g., carbapenems, polymyxins, tigecycline, cefiderocol), for a duration of at least 48 hours.

Comparator Not applicable – this is a single-arm meta-analysis of studies where all patients received SUL-DUR (no active comparator or placebo group required).

Study designs to be included Prospective or retrospective case reports, case series (including those reported as meeting abstracts), and the published phase 3 randomized controlled trial (ATTACK trial). Reviews, editorials, in vitro studies, and studies without original clinical outcome data were excluded.

Eligibility criteria Inclusion criteria (additional):

Studies published in English or Chinese (no other language restrictions applied).

Studies with full-text available or sufficient data reported in the abstract (for conference abstracts) to allow extraction of outcome data.

Studies reporting at least one of the outcomes of interest (overall survival or microbiological clearance).

For case series, minimum sample size of 1 patient (i.e., single case reports were eligible).

Exclusion criteria (additional):

Studies that did not provide original clinical outcome data (e.g., reviews, editorials, letters, comments, consensus reports).

In vitro studies, animal studies, pharmacokinetic/pharmacodynamic studies without clinical outcomes.

Studies where CRAB infection was not confirmed by microbiological testing.

Studies with mixed infections (e.g., CRAB co-infection with other pathogens) where the effect of SUL-DUR on CRAB could not be isolated.

Duplicate publications: when the same patient cohort was reported in multiple articles, only the most recent or most complete report was included.

Studies with insufficient data to calculate the event rate (e.g., no denominator or numerator for survival or clearance) and no response from corresponding authors after contact.

Studies with treatment duration < 48 hours.

Studies exclusively in pediatric patients (<18 years) unless part of a mixed adult-pediatric cohort where adult data could be extracted separately.

Information sources The following electronic databases were systematically searched: PubMed/MEDLINE, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang Data Knowledge Service Platform, and VIP Chinese Journal Service Platform (VIP), from database inception to March 31, 2026. To ensure comprehensiveness, we also searched international conference abstracts including ASM Microbe, the European Congress of Clinical Microbiology and Infectious Diseases (ESCMID), and the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), and manually screened the reference lists of included studies to identify additional relevant articles.

Main outcome(s) The primary outcome was overall survival, defined as survival to hospital discharge, 28-day survival, or clinical cure as reported by the original studies. The secondary outcome was microbiological clearance, defined as negative follow-up culture from the primary infection site after treatment. The effect measure for both outcomes was the pooled proportion with its 95% confidence interval. For survival, the timing varied across studies (mostly 28-day or in-hospital

survival); for microbiological clearance, assessment was typically performed at the end of therapy or at test-of-cure (7±2 days after the end of treatment). All analyses were conducted using the generalized linear mixed model with a random-effects assumption.

Quality assessment / Risk of bias analysis The quality of individual studies was assessed using the National Institutes of Health (NIH) Quality Assessment Tool for Case Series Studies. This tool includes nine items evaluating: (1) clarity of the research question, (2) clear definition of the study population, (3) consecutive collection of cases, (4) prospective or complete ascertainment of outcomes, (5) objective measurement of exposure, (6) sufficient follow-up duration, (7) clear definition of outcomes, (8) appropriate statistical analysis (if applicable), and (9) adequate reporting of losses to follow-up. Each item was rated as "yes" (1 point), "no" (0 points), or "not applicable/not reported". Total scores were categorized as high quality (≥7), moderate quality (5–6), or low quality (≤4). For the single randomized controlled trial (ATTACK trial), the Cochrane Risk of Bias 2.0 tool was used to assess five domains: randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results. Conference abstracts were assessed for completeness of reporting (sample size, intervention, outcomes) because standard quality tools could not be applied. All assessments were performed independently by two reviewers, and disagreements were resolved by discussion or by a third reviewer.

Strategy of data synthesis All statistical analyses were conducted using R software (version 4.5.0). The primary outcome was overall survival, and the secondary outcome was microbiological clearance. Both outcomes were expressed as pooled proportions with 95% confidence intervals (CIs).Because the included studies were mainly case reports and case series with small sample sizes (some with only one patient), we used a generalized linear mixed model (GLMM) with a random intercept logistic regression as the primary analytical approach. This method directly models the binomial distribution and does not require continuity correction for zero events, making it suitable for rare events and small studies. Heterogeneity was assessed using the I^2 statistic and Cochran's Q test. I^2 values 50% high; the significance level for the Q test was set at $P < 0.10$. To evaluate the robustness of the pooled estimates, a leave-one-out sensitivity analysis was conducted by sequentially removing each study and recalculating the pooled proportion. Publication bias was examined using funnel plots and Egger's regression test. Asymmetry was assessed by visual inspection of the funnel plot, and Egger's test ($P < 0.10$) was considered indicative of significant bias. If publication bias was detected, a trim-and-fill method was applied to estimate the adjusted pooled proportion.

All tests were two-sided, and a significance level of $\alpha = 0.05$ was adopted.

Subgroup analysis Subgroup analysis was performed according to infection site (single-site versus multi-site).

Sensitivity analysis To assess the robustness of the pooled estimates, several sensitivity analyses were performed.

First, a leave-one-out sensitivity analysis was conducted by iteratively removing one study at a time and recalculating the pooled overall survival rate. This method allowed us to evaluate whether any single study had a disproportionate influence on the summary estimate.

Second, we restricted the meta-analysis to studies with a sample size of ≥10 patients (i.e., the ATTACK trial and the larger case series). This analysis aimed to examine whether small case reports skewed the pooled results.

Third, we repeated the meta-analysis using a fixed-effect model (instead of the random-effects GLMM) to compare the consistency of the effect estimates under different modelling assumptions.

Fourth, a subgroup analysis excluding case reports was performed to assess the impact of including only higher-quality evidence (case series and the RCT).

All sensitivity analyses were performed for both the primary outcome (overall survival) and the secondary outcome (microbiological clearance) whenever data allowed. The results of the sensitivity analyses were considered supportive if the direction and magnitude of the pooled estimates remained similar to those of the main analysis.

Country(ies) involved China.

Keywords Carbapenem-resistant Acinetobacter baumannii; Sulbactam-durlobactam; Overall survival; Microbiological clearance; Meta-analysis; Case series; Single-arm meta-analysis.

Contributions of each author

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