Reviewer's report

This manuscript assesses the comparative efficacy of amoxicillin–clavulanic acid versus ertapenem in a rat model of peritonitis induced by ESBL-producing *Escherichia coli*, with the aim of exploring carbapenem-sparing therapeutic strategies. The study addresses a clinically relevant and timely question in the context of rising antimicrobial resistance and antimicrobial stewardship. However, I believe this work could be improved through the following points:

1. L40: Considering the model used in this study (animal), the small sample size, and the lack of resistance emergence analysis, I suggest that the authors rephrase the abstract's conclusion to emphasize preclinical evidence and antibiotic-sparing potential, not treatment recommendations. Suggestion: "Findings from this experimental study suggests comparable efficacy of AMC and ertapenem in reducing inflammation and bacterial burden…"
2. In the Abstract and Introduction sections, the authors emphasized spontaneous bacterial peritonitis (SBP) in cirrhotic patients, yet the study uses a non-cirrhotic rat model without ascites. This disconnect should at least be acknowledged or justified.
3. I suggest that the authors clearly outline the concept of "non-inferiority" and its relevance to this study in the Introduction or avoid the term and use more appropriate exploratory language.
4. While antimicrobial resistance is introduced broadly in the Introduction section, the specific problem of carbapenem overuse and selection pressure is not clearly articulated. The authors should clearly frame the study within the context of antimicrobial stewardship, emphasizing the risks of carbapenem overuse (resistance amplification, ecological impact), and the clinical interest in narrower-spectrum alternatives for ESBL infections.
5. Line 65: This "IDSA 2024 Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections(8)" appears as a standalone sentence fragment with no explanation.
6. Line 72: The discussion on animal models should be critically expanded to include the rationale for choosing direct inoculation over caecal ligation, suitability of animal models for antimicrobial efficacy studies, and other important concepts to improve the rigor of the section.
7. Line 77: "Mural model" or "murine model"?
8. Line 102: Could the use of talc to prevent spontaneous healing not artificially amplify inflammation and bias treatment effects? The authors should provide a stronger justification for this.
9. Section "3.3" was labelled twice.
10. The small sample sizes, particularly in the sham group and the proteomic subsamples, substantially limit the statistical power of the study. As a result, several key interpretations in the Discussion section such as superior peritoneal diffusion of amoxicillin–clavulanate, systemic efficacy, and control of bacteremia are based largely on non-significant trends

rather than robust statistical evidence. In addition, mortality outcomes are not informative, as only a single death occurred.

11. While the Discussion frequently attributes the absence of statistical significance to limited sample size, strong conclusions as highlighted above were still drawn from them, which represents a major interpretative inconsistency that should be addressed.
12. The authors repeatedly extrapolate findings from the talc-induced rat peritonitis model to human ESBL spontaneous bacterial peritonitis, without sufficiently acknowledging the inherent biological and clinical limitations of this experimental system. Such overextension of conclusions from an artificial animal model to human disease is problematic and should be substantially tempered.
13. The manuscript should be thoroughly proofread and edited to address several grammatical inconsistencies and improve coherence.