Reviewer’s report

Title: Quantifying the clinical virulence of Klebsiella pneumoniae producing carbapenemase Klebsiella pneumoniae with a Galleria mellonella model and a pilot study to translate to patient outcomes

Version: 2
Date: 29 November 2013
Reviewer: Jason J Pogue

Reviewer’s report:

I commend McLaughlin and colleagues for their revised submission. I find that the presentation of the data follows a more logical progression, and the authors do an excellent job of explaining the novel methodology. Furthermore, they do a nice job of emphasizing throughout the exploratory nature of the translational model and the limitations imposed by the lack of power. The revised manuscript present a few new issues that need addressed, but presuming the authors can appropriately address, these data warrant publication.

- Major/Minor Compulsory Revisions

Page 7, line 130- please define time to active therapy as different publications have different definitions. Additionally, if the patient received a carbapenem, and it had in vitro activity, was that considered active? I don't think the authors need to justify that one way or the other as the data are mixed, but they need to define for the readership

- Line 147 and throughout- the authors frequently talk about carbapenem use post culture. It is also added to the models, however, there is no real explanation for why. I am unclear the relevance.

- Line 217-219: The authors do an excellent job in the revision explaining the interplay between the virulence score and mortality, suggesting that virulence had no impact on mortality (and perhaps actually associated with a decrease)! This is an extremely important finding, and well described. The authors also point out in their models the importance of APACHE II and mortality. The one aspect that the authors do not comment on, that could still significantly impact mortality is therapy. There have been multiple studies showing the improvement of combination therapy over monotherapy for the treatment of KPC bloodstream infections. Also, assuming these patients received colistin therapy- the question of dosing would inevitably come up. To be fair to the authors, the sample size is too small to truly delve into these complex issues, but I do believe they could/should do two things: 1) describe the definitive regimens that patients with KPC received and 2) Add a quick blurb on this to the discussion (how optimal therapy remains undefined, and the impact of that on survival cannot be assessed in this study)

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests: I declare that I have no competing interests