Reviewer’s report

Title: Daptomycin in experimental murine pneumococcal meningitis

Version: 1 Date: 23 February 2009

Reviewer: Stephen Leib

Reviewer’s report:

The paper by Mook-Kanamori et al reports results from a study comparing vancomycin vs daptomycin in treatment regimen including adjuvant dexamethasone in an adult murine model of pneumococcal meningitis. The main finding of the study was that daptomycin and vancomycin given in combination with dexamethasone did not show significant differences in bactericidal activity. The authors conclude that further studies are needed to investigate the effects of daptomycin but that their results are consistent with previous findings supporting the evaluation of daptomycin as an alternative to vancomycin for the treatment of bacterial meningitis.

The paper addresses an important disease where treatment options are limited. The main finding, a similar bactericidal activity of daptomycin and vancomycin under a dexamethasone containing treatment regimen for pneumococcal meningitis is important and novel. The study is well conceived and performed and paper is clearly written, concise and the conclusions are appropriate.

- Minor Essential Revisions

A few questions may need clarification:

1. Was the mortality rate of the model 0%? Did all infected mice survive until 24 h after infection?

2. Line 115: The whole brain sections where scored for inflammation, neuronal necrosis, and apoptosis...". Please state of which cells apoptosis was assessed. How was inflammation scored?

3. Line 165: "The amounts of inflammation and apoptosis of brain parenchymal cells where equivalent..."This finding is rather unexpected and is somewhat contradicted by the data presented on line 170-172 "the density of bacterial cocci...appeared to be lower...". Here the presentation of the data on "inflammation and apoptosis of brain parenchymal cells" and a statement on the methods used for quantification of bacterial density would be helpful for interpretation of the findings discussed on lines 229-233.

4. Table 1 and Figure 3: Data at 0 hours is lacking in the table on groups dexamethasone/ plus antibiotics while data is presented in Figure 3. Has the data at 0 h been pooled from all treatment groups? Please clarify.
- Discretionary Revisions

Abstract and elsewhere: "intrathecally" could be replaced by "Into the cisterna magna" or "intracisternally"

Lines 87-88 and 92-93: Duplicate statement of: "96 animals where divided into..."

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests