Reviewer's report

Title: High-dose daptomycin and fosfomycin treatment of a patient with endocarditis caused by daptomycin-nonsusceptible Staphylococcus aureus: Case report

Version: 1 Date: 29 November 2010

Reviewer: Warren Rose

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Major Compulsory Revisions
1. No balance is given to the activity and use of fosfomycin against staphylococci, including MRSA. Although high dose daptomycin use in treating non-susceptible strains is interesting, this has been reported previously. The most interesting aspect is the use of fosfomycin, for which the authors failed to give proper introduction to the reader. Review of this could be done in just a few sentences in the introduction.

2. Some of the references in the introduction and conclusion do not seem to properly support the statement given. There are many examples throughout, but one introduction example is referencing the 6-8 mg/kg dose for S. aureus bacteremia and endocarditis with a reference from 2004, two years before dosing in this disease state was established in clinical trials. A careful review of all references is needed, and authors should adjust accordingly.

3. The timeline of the disease-treatment course is unclear. Can the authors provide specifics to the duration of treatment for each course (Ex: how many days was the patient on vanco and linezolid therapy, daptomycin therapy?)

4. Using broth dilution is not an approved standard for fosfomycin susceptibility testing. Did the authors also perform agar dilution testing (recommended standard) of control strain for verification?

Minor Essential Revisions
1. There is no sufficient evidence for daptomycin as an option for hVISA and VRSA. This statement should be revised to state daptomycin as a treatment option for staphylococcus aureus endocarditis, including MRSA.

2. For susceptibility testing of fosfomycin, was 25 mg/L of glucose-6-phosphate added to the media as indicated by CLSI?

3. In the second paragraph of the conclusion, authors state that isolate st06 was susceptible to daptomycin in combination with fosfomycin. This indicates that synergy testing was performed. If so no results are given.

Discretionary Revisions
1. Authors could mention the effects of the mutational genes identified in dapto-NS. Ex: membrane fluidity changes and others (Jones T. Antimicrob
Agents Chemother 2008)

2. Although no CLSI interpretive standards are given for fosfomycin MICs in S. aureus, EUCAST breakpoints exist for staphylococci (susceptible \( \leq 32 \) mg/L) and would help add some relevance to the MICs reported in the paper.

**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:**

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- consultant
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Medicines Company
- consultant