Reviewer's report

Title: An open-label, pragmatic, randomized controlled clinical trial to evaluate the comparative effectiveness of daptomycin versus vancomycin for the treatment of complicated skin and skin structure infection

Version: 2
Date: 24 April 2015
Reviewer: Richard Brindle

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Minor essential revisions

Table 2 should have ‘hours’ rather than ‘h’
Table 3
I could not work out the figures for Staphylococcus aureus in the ‘By pathogen’ section; the daptomycin arm had 39 MRSA and 14 MSSA = 53 but in the S. aureus column the figure was 58 with a statement that 4 daptomycin patients had other infection types (what does this mean?). The figures for MSSA were similarly confusing. It also states (subscript e) that the S. aureus column contains coagulase-negative staphylococci. This section needs to be clearer and perhaps the S. aureus column should be called Staphylococcus.spp, if the authors consider these to be significant?

I could not find a funding statement. I assume the study was funded by Cubist but it should state it.

Discretionary revisions

Table 1 is long and one wonders whether Race could not be removed as it is not hypothesised that race has any relationship to outcome in SSSIs.

It is not clear how the study patients were selected to need IV therapy or how the investigator would anticipate the duration of IV therapy.

No definition of complicated cellulitis.

A more rigorous vancomycin dosing procedure would have been helpful - ‘Vancomycin was dosed at the investigator’s discretion’. Perhaps a statement as to why it was not standardised as was daptomycin.

The length of stay measurements are a bit confusing as hours are used for primary outcome but days in the sample size calculation and most of the text.

It is not clear how the infection-related LOS was determined from the total LOS.

The greater prior use of vancomycin in the daptomycin arm and its effect on faster clinical success in the daptomycin arm was not discussed.

Are the discussion and conclusions well balanced and adequately supported by the data?
Generally; Yes. One could argue that for the relatively short length of stay, daily vancomycin levels were unnecessary.

The paper suggests that length of stay could be abbreviated and replaced by outpatient parenteral antibiotic therapy but does not consider whether the inpatient stay could be reduced by treatment with oral agents e.g. trimethoprim-sulfamethoxazole or clindamycin.

The statement ‘… data suggests that health care provider and patient preference …. should be the primary driver for initial antibiotic selection’. It does not describe how one should decide which agent to prefer. If daptomycin is not demonstrated as superior in terms of clinical success and results in a potentially more expensive hospital stay, why should the health care provider or patient prefer it?

Are limitations of the work clearly stated?
Yes. However, the authors do not discuss the issue of this being an unblinded study and whether this might have affected the assessment of success.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:
I am doing a Cochrane review of cellulitis and this paper contains data that may be relevant to that review.