Reviewer’s report

Title: Telavancin versus standard therapy in patients with uncomplicated Staphylococcus aureus bacteremia: the ASSURE Study

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Reviewer: Maria Helena Rigatto

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Article review
Title: “Telavancin versus standard therapy in patients with uncomplicated Staphylococcus aureus bacteremia: the ASSURE Study.”

The study aims to answer an important question regarding therapeutic options for S. aureus bacteremia. This is a topic of major importance specially considering the challenges imposed by standard therapy to methicillin resistant S. aureus with vancomycin. It’s a well-written article with overall adequate description of its methods and results.

Some considerations bellow:
- Discretionary revisions
  • The title could include the study design: a randomized clinical trial, proof of concept study, following CONSORT recommendations.
  • The introduction clearly explains the background for the study and its main question and hypothesis. However it could be shortened to two or three paragraphs. It’s given a detailed explanation about challenges with vancomycin therapy; nevertheless the study is not designed to compare telavancin specifically with vancomycin. This information could be resumed once it’s not the main focus of the study.
  • Results section
    o Much of the data provided in the text is already described on the tables and does not need to be repeated- just reference the tables.
    o Information from table 1 could be suppressed as it mostly repeats data from figure 1. Table 4 essentially repeats data from the text and from table 2.
- Minor essential revisions
  • Results section
    o Data presented on the results section do not match exactly with the ones presented on figure 1 and should be checked: 1) It’s described on the text that 58 patients were randomized, but in fact 60 patients were randomized and only after it was defined which was the all treated population. 2) the text mentions 5 patients with positive follow up blood culture in telavancin group, but the figure...
shows 8 patients 3) the text mentions that “55% of patients in the telavancin group and 41% in the standard therapy group discontinued the study drugs due to failing > 1 continuation criteria”, nevertheless according to the numbers presented in the figure the ones that discontinued were 14/29 (48.3%) in telavancin group and 13/29 (44.8%) on standard therapy group.

- Major compulsory revisions

- Methods section
  - Randomization - it is described that it was done by interactive voice response system. It is not mentioned though which method was used to generate the random allocation sequence and if it was stratified by center. Once the study was performed in 21 sites, heterogeneity of the sites could directly influence outcomes.
  - Blinding - It’s a double-blind study, however it’s not described how blinding was performed. There are some challenges in this case like different posology of the drugs and eventually the need to collect specific exams like vancomycin serum level.
  - Inclusion, exclusion and continuation criteria are well described. The authors could comment why it was chosen to include also MSSA bacteremia treated with anti-staphylococcal penicillin. The main challenge of current therapy is to MRSA and it’s possibly the situation where having telavancin as an option would bring more advantages so why to include MSSA strains.
  - Sample Size - it’s mentioned that sample size was selected on the basis of clinical judgment which is fine, however it’s not described which was the previously expected sample and based on what parameters.

- Results section
  - Table 5 shows that only 2 patients had acute renal failure in telavancin group, however in table 6, 7 patients are presented as having creatinine increase. How was acute renal failure defined? Why didn’t the authors evaluate acute kidney injury by a standardized score, like RIFLE or AKIN, instead of defining it as 50% of creatinine increase.

- Discussion section
  - Although in the test-of-cure visit of the clinically evaluable group cure rates were similar, when analyzing the all treated population cure rates were higher in standard therapy in all evaluation periods. There was no statistically significant difference probably due to the small sample, but certainly there was a trend of better results for standard therapy group. This should be emphasized on the discussion.
  - Not only general adverse events were higher in telavancin group but also the serious ones. That could have been underestimated by the small sample and should also be emphasized in the discussion.
  - As mentioned by the authors the small sample size and heterogeneity in local policies for administration of standard therapy, especially vancomycin, are clear
limitations of the study. Results must be interpreted with extreme caution specially considering lower cure rates in the all treated population and the higher number of adverse events in telavancin group.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests