Reviewer's report

Title: A randomized trial of tigecycline versus ampicillin-sulbactam or amoxicillin-clavulanate for the treatment of complicated skin and skin structure infections

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Reviewer: RAVINA KULLAR

Reviewer's report:

Matthews P., et al. A Randomized Trial of Tigecycline versus Ampicillin-Sulbactam or Ampicillin-Clavulanate for the Treatment of Complicated Skin and Skin Structure Infections.

Peters et al. performed a randomized, open-label study comparing tigecycline vs. ampicillin-sulbactam or ampicillin-clavulanate (with the addition of vancomycin to the control if infection with MRSA was suspected or confirmed)

Major Compulsory Revisions:

1. Introduction – overall, the introduction section is very abbreviated. The authors could expand this by discussing in further detail about CA-MRSA, especially since the authors choose to distinguish between HA-MRSA and CA-MRSA via mec typing. What does the current literature state about SCCmec IV vs. SCCmec II and CA-MRSA vs. HA-MRSA? Would also expand on the coverage of tigecycline. What do the IDSA guidelines state about the role of tigecycline for MRSA infections?

2. Methods (under “Subjects”; 1st paragraph) – authors need to clarify what is meant by “complicated underlying disease.”

3. Methods (under “Efficacy and Safety Evaluations”; 2nd paragraph) – was any other molecular testing performed? PVL production? Lineage (USA300, etc)?

4. Methods – General comment. Did the authors look at clonal identity for the MRSA strains, especially those collected in the same year. Even though the authors selected unique patients, this does not mean there has not been dissemination of the same clone.

5. Results (under “Patient Characteristics”; 1st paragraph). What was the median (IQR) duration of therapy the comparator group received vancomycin therapy? What was the median initial vancomycin trough concentration?

6. Results – General comment. Did any patients in the tigecycline group receive combination therapy? If so, what combination?

7. Table 1- there was no measurement of severity of illness such as APACHE II scoring.

8. Table 1 – what prior antibiotics that patients failed on were these patients on?

9. Results (under “Safety and Tolerability”; 1st paragraph). It is concerning that
patients in the tigecycline group experienced more nausea, vomiting, and diarrhea. What is the breakdown of these adverse events by pathogen?

10. Discussion – overall, the discussion is brief. Can be expanded by discussing about the limitations of other therapeutic agents approved for cSSSIs and MRSA infections. What makes tigecycline an ideal agent to choose above other agents for cSSSI? Appears to be no discussion of this.

Minor Essential Revisions:
1. Methods (under “Subjects”, 2nd paragraph) – how did authors handle patients with spontaneous drainage? Define uncomplicated skin infections.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**
I serve on the Speaker's Bureau Cubist Pharmaceuticals.