Reviewer's report

Title: Cardiac events after macrolides or fluoroquinolones in patients hospitalized for community-acquired pneumonia: post-hoc analysis of a cluster-randomized trial

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Reviewer: Aran Singanayagam

Reviewer's report:

A large study on an important topic from a post-hoc analysis of the CAP-START trial. The paper is well written and the authors don't over-state the interpretation/conclusions they make which is important. The statistical testing used in complex and (in some places) beyond my expertise so I would suggest a reviewer with statistical expertise evaluates the manuscript also. I have the following suggestions for consideration:

1. Given that the main signal they see is heart failure, it would be useful to have a bit more detail on how the authors distinguished true acute left ventricular failure (i.e. a cardiac event) from a sepsis-induced picture. Did any of the patients classified have echo or BNP? Could they carry out a sub-analysis of such patients?

2. The authors have adjusted for some important variables that could influence outcomes in the multi-variable analyses. However, given that cardiac events are a key endpoint, they should consider use of medications such as statins, anti-platelets and smoking history.

3. The term 'heart failure' should be described more accurately throughout the manuscript? e.g. Acute? Chronic congestive? Left-sided? Right-sided?

4. For any tables (e.g. table 1) or descriptions in the text where %s are compared, it would be helpful to show p values to indicate where significant differences exist.

5. The authors speculate a hypothesis for why erythromycin could be associated with heart failure (volume and sodium load). My thoughts would be that it is more likely to be arrhythmia-induced failure that is occurring more often in erythromycin patients. Do they have any data on co-occurrence of arrhythmia and heart failure in individual patients?

6. Table 1 should show other factors of importance to cardiac events/arrhythmias e.g. alcohol excess, thyroid diseases, current or previous smoking etc
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
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