Author's response to reviews

Title: Inappropriate empiric antifungal therapy for candidemia in the ICU and hospital resource utilization: a retrospective cohort study

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Author's response to reviews:

Dear Dr. Norton,

We thank you once again for giving us an opportunity to improve our work further. Below are our responses to Dr. Gangneux's comments.

Sincerely,
Marya Zilberberg, MD, MPH

Reviewer's report

Title: Inappropriate antifungal therapy for candidemia in the ICU and hospital resource utilization: a retrospective cohort study
Version: 2 Date: 27 April 2010
Reviewer: jean-pierre Gangneux

Reviewer's report:
This topic is interesting. The manuscript is well written and discussion is adequately supported by the data obtained in a cohort of patients and after modelization.
A prospective study would have been more powerful.

- Major Compulsory Revisions
1. The authors did not define enough the inappropriate therapy:
   - delay of > 24h : after positive culture? after yeast identification?
AU: At the top of page 5, we stated that the delay was after the onset of candidemia, and the treatment was empiric.
- inadequate dose: what dose for fluconazole, 800 mg/d?
AU: We have now added the following for clarification on page 5:
“Adequacy of the dose was based on the dosages recommended by the Infectious Diseases Society of America and the individual antifungal package insert. The initial adequate dosage of fluconazole for susceptible isolates was defined as 6 mg/kg/day for Candida albicans, Candida tropicalis, and Candida parapsilosis in the face of normal renal function, and 3 mg/kg/day if creatinine clearance was < 50 ml/min. Fluconazole was not considered to be adequate at any dosage for Candida krusei or Candida glabrata.”

- why is the inappropriate drug a third point?
AU: We are not sure what the reviewer is referring to.

2. Please clarify in the title that the study of the inappropriate treatment concerns empiric (or probabilist) therapy and no the curative therapy.
AU: We have now added the word “empiric” to the title.

What drugs are used in case of empiric therapy in their hospital?
AU: Please, see the expanded statement on prophylaxis and empiric treatment at BJH on page 4.

3. The authors gave the crude mortality, is the attributable mortality available?
AU: To arrive at attributable mortality, we would need to perform a case-control study. The current design is a cohort study.

4. Can the authors specify the main causes of increased LOS: persistent fever secondary localization? etc...
AU: The reviewer asks an important question. Unfortunately, we do not have sufficient granularity of data to answer it.

5. B-D-glucan detection is considered as rapid and promising diagnostic tool, however, it can not discriminate between yeasts and filamentous fungi, and therefore doesn't allow the adaptation of the therapy to the fungus isolated before culture.
AU: Thanks for this comment.