Author's response to reviews

Title: Safety and efficacy of amphotericin-B deoxycholate inhalation in critically ill patients with respiratory Candida spp. colonization: a retrospective analysis.

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Author's response to reviews: see over
Dear Sheryl Ramos,

Thank you for the quick reviewing process and the comments of the reviewers. Below you will find a point-by-point response to these comments. Any changes made are noted in the response and highlighted in the accordingly revised manuscript.

**Reviewer 1 (Shirish Huprikar):** thank you for your comments.

1. The authors need to better clarify any literature that provides any scientific foundation for this practice (use of nebulized amphotericin B).

   The data for this study where obtained from a tertiary intensive care unit in the Netherlands which uses selective decontamination of the digestive tract (SDD). SDD is used to eradicate *Candida* species from the lower respiratory tract using topical amphotericin B. Nebulized amphotericin B is added to this regimen in order to eradicate *Candida* species in patients with persistent *Candida* colonization despite using the topical amphotericin B. This regimen has now been used for several years, however the clinical effectiveness of this approach in reducing the burden of *Candida* colonization in ICU patients is not known. There is some literature describing this widespread practise for SDD (De Jonge et al., ref 14 and De Smet et al., ref 15), both studies observed an improved survival in patients using SDD. However there is no scientific evidence for the use of nebulized amphotericin B in the SDD regimen (see also Ong et al., ref. 16).

   The articles of De Jonge et al. and De Smet et al. are implemented in the introduction as references.

**Reviewer 2 (Evangelos Giamarellos-Bourboulis):** thank you for your comments.

1. I cannot understand the repetitive need to indicate in the Figure and Table legends and in the context of the tables, the split of the ABDC group into time from colonization to therapy and from time to therapy until final outcome.

   We understand the described problem caused by the non-randomized nature of this study. We wanted to evaluate baselines up to start of treatment in the ABDC group and therefore split the data before and after start of treatment on day 5 (5) in the
treated group, since treatment was initiated at median day 5 (5). To evaluate the effect of treatment we used the data after day 5 (colonization lasted 5 (9) days in the untreated group and treatment was initiated at median day 5(5) for the treated group) for both groups (figures). We skipped Table 3 which is less informative. Otherwise data were presented in tables starting from day 1 of colonization.

The results section has partly been rewritten.

2. I would prefer to see Figures 2 and 3 with the curves moving cumulatively upwards to the right instead of the current survival design.

We made new Figures with the curves moving cumulatively upwards to the right.

Figure 2.
Figure 3.

Sincerely,

Patrick van der Geest M.D.