Author’s response to reviews

Title: Serum (1-3)-β-D-Glucan and Galactomannan Levels in Patients with Cystic Fibrosis: a Retrospective Cohort Study

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Point to point reply:

Reviewer #3

Comment by the reviewer: “Please, add a mutation list of the included CF patients and pancreas status.”

Response: The ethics committee of the University of Erlangen has waived the need for informed consent because the study was retrospective and no additional samples had to be taken. However, the ethical approval did not cover the use of genetic data of the patients without informed consent. Therefore, we apologize that we cannot provide the information requested by the reviewer.

The information on pancreas status is included in table 1.

Comment by the reviewer: “I would like to recommend in terms of determination the grade of pulmonary obstruction to discriminate between FEV1/VC >80% and below 80%. FEV1 alone is too narrow.”

Response: We have searched the patients’ records for the vital capacity in order to use the Tiffeneau index instead of the FEV1 for classification. However, in a considerable number of patients the information was not documented. As a consequence of the retrospective design of
our study we apologize that we cannot provide this information and follow the reviewer’s suggestion.

The existing studies on (1→3)-β-D-glucan and galactomannan in CF patients (Rautemaa et al. [1] and Warren et al. [2]) used the FEV1 and not the FEV1/VC as lung function parameter. For better comparability it is therefore beneficial to keep the FEV1-based classification.

However, we are very thankful for this information and will use the FEV1/VC in subsequent studies.

Comment by the reviewer: “I would like to recommend showing FEV1 (%pred.) and GM correlations as a graph, it provides better readability than a table.”

Response: We followed your advice and included the graph as figure 1 in the manuscript.

Comment by the reviewer: “Have you also determined GM sputum levels? If not, please, comment on this. Do sputum levels offer a more specific answer to your questions? If there is Aspergillus in the airways, do we always find GM in the airways?”

Response: No, we did not measure sputum GM levels. Unfortunately, there are no archived sputum samples available for GM testing or Aspergillus-PCR. The sensitivity of sputum GM is higher than the sensitivity of culture. Therefore, it could have an impact on our study. It seems plausible that Aspergillus culture-negative but GM-positive patients are less heavily colonized in comparison to the Aspergillus culture-positive patients. With regard to our study, this could mean that there is an additional patient population with low-level Aspergillus-colonization within our Aspergillus culture-negative group. The crucial question is how the serum BDG and GM levels in this population are. If they are negative the number of false-negative patients in our study will increase and if they are positive some of the false-positive patients will be transformed into true-positive patients. However, the sensitivity of sputum GM is also limited and there will be an unknown number of patients with negative GM and Aspergillus-colonization. Perhaps Aspergillus-PCR could identify those Aspergillus culture- and sputum GM-negative Aspergillus-colonized patients.

We have discussed this issue in the revised manuscript (page 14, line 344-351).
