Author’s response to reviews

Title: Successful Eradication of Newly Acquired MRSA in Six of Seven Patients with Cystic Fibrosis Applying a Short-Term Local and Systemic Antibiotic Scheme

Authors:

Alexander Kiefer (alexander.kiefer@uk-erlangen.de)
Christian Bogdan (christian.bogdan@uk-erlangen.de)
Volker Melichar (volker.melichar@uk-erlangen.de)

Version: 1 Date: 15 Jul 2017

Author’s response to reviews:

We are grateful to the editor and the reviewers for their helpful comments on our manuscript. As detailed below, we have carefully followed the various suggestions and changed/amended the manuscript accordingly.

Ad Editor comments:

We changed the discussion section and table 4 (former table 3) to comment on the mentioned publication of Muhlebach et al.

Ad Reviewer 1:

1. We changed the discussion section and table 4 (former table 3) to comment on the publication by Muhlebach et al. 2017.

2. As our eradication protocol was performed under inpatient hospital conditions, the adherence to therapy was supervised by nurses and was confirmed to be good. However, we did not assess the adherence in a standardized manner which is a weakness of our study. On the other hand, none of our patients refused to undergo the outlined MRSA eradication protocol or interrupted the therapy which underlines the compliance and acceptance by the patients. Moreover, other reported MRSA eradication protocols are much more intense, e.g. Kappler et al. (3 weeks of dual intravenous and 6 weeks dual oral antibiotic treatment) [Kappler M, Nagel F, Feilcke M, Kroner C, Pawlita I, Naehrig S, et al. Eradication of methicillin resistant Staphylococcus aureus detected for the first time in cystic fibrosis: A single center observational study. Pediatr Pulmonol. 2016 Jul 5. doi: 10.1002/ppul.23519.]
3. We have added this issue to the discussion section of our paper.

4. We believe that carrying out the eradication protocol at home would lead to a significantly lower success rate. However, as our study did not include a control group which underwent the eradication protocol at home, this remains to be formally demonstrated. In Germany, the inpatient hospital stay is covered by the health insurances. Therefore, we have to admit that this protocol may not be feasible in other countries.

5. The genotype data has been added to Table 2.

6. The title of figure 1 has been changed as proposed by the reviewer.

7. As the patients were recruited at different times and due to the retrospective setting of the study, the follow-up period varied. As requested we have now included the length of the follow-up period in table 3.

8. Although a positive effect on pulmonary disease and lung function parameters is not proven yet, there are other issues that have to be considered. Because of the contact precautions which are necessary for patients with chronic MRSA colonization, they are often unable to receive important therapeutic measures which are part of the routine treatment for CF patients in Germany. In particular, the outpatient physiotherapy which is performed once a week by a specially trained physiotherapist and the rehabilitations are often withheld from the patients. This might be different in other countries, but in our opinion this is an important reason to eradicate MRSA.

9. Unfortunately we have no quantitative bacteriology data and did not collect inflammatory biomarkers as the MRSA was detected in routine monitoring. We have now specified this in the method section.

Ad Reviewer 2:

1. In the background section of our paper we commented on the impact of chronic colonization with MRSA in patients with cystic fibrosis in order to explain why we attempt an early eradication. In the method section, we indeed incorrectly used the term “newly infected”. We have now changed it to “newly colonized” which in our opinion is the correct term.

2. Since 2012 every patient who newly acquired MRSA was offered eradication by our established protocol and none of the patients refused to be admitted to the hospital. Each of these patients was followed up at our CF center with sputum analysis or oropharyngeal swab
at least every three months. The period of follow up varied from patient to patient due to the retrospective design of our study as mentioned in the result section and in table 3.

3. Newly acquired colonization with MRSA was defined by one culture positive for MRSA, either derived from sputum or oropharyngeal swab. Unfortunately, not all patients had the same modality of microbiological analysis to confirm eradication; especially the younger patients were not able to produce sputum at each of the scheduled control analyses. Therefore, we changed the text as proposed by the reviewer.

4. We have added this point to the discussion section of our paper.

5. We have now included the discussion of the proposed published literature that suggests that MRSA eradication is not associated with a change in the decline of pulmonary function.

6. We changed the result section of our paper as proposed by the reviewer, specified the rate of change in FEV1% predicted in table to and removed figure 2.

7. The genotype has been added to Table 2. Likewise, an indication for disease severity can be deduced from the age in conjunction with the FEV1 % predicted value at the time of newly diagnosed MRSA colonization as given in table 2.

8. The microbiological analysis using either sputum or oropharyngeal swabs, was part of our routine check-up of the patients, which in our CF center is performed at least every three months. We have now added this information to the method section of the manuscript. As the patients had no specific symptoms indicative of MRSA infection, a clinical improvement could not be detected. As already mentioned in the comment to point 1 we changed the terminology from “newly infected” to “newly colonized” because the original term was misleading.

9. We changed the discussion section and table 4 (former table 3) to comment on the publication by Muhlebach et al as requested.