Peer Review File

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Review Comments

Reviewer A

The authors have reported the usefulness of EC-based combination therapy in patients with treatment-resistant PJP, with a good literature review.

However, there are some additional critiques as follows:

Minor Compulsory Revisions:

Comment 1: How long should EC-based combination therapy be continued? It was unclear why the authors decided to stop micafungin + clindamycin treatment after 8 days (D20–D28). In addition, I wonder if the pretreatment (TMP/SM, primaquine + clindamycin) might be partially effective; in that case, EC-based salvage therapy might not be necessary.

Response 1: We thank the reviewer for this suggestion. We have added a paragraph at the end of the discussion to address this. We selected our duration of therapy based on timing of intolerance and difficulties liberating the patient from mechanical ventilation. Ultimately, we chose 6 days (corrected errors on timeline) as this completed a full 21-day course for PJP and the patient had clinically improved at the end of the 21 days.

Changes to the text: See last paragraph of discussion section, page 11 lines 5-17 and discussion about Huang et al on page 10, lines 1-14.

Comment 2: In the Discussion section, the authors should explain why EC treatment durations differ from report to report.

Response 2: We thank the reviewer for this suggestion. We have added a paragraph at the end of the discussion to address this. The optimal duration of echinocandin therapy has not been studied. The duration of therapy in other reports ranges from four to 24 days, which is based on the timing of intolerance and remaining duration of therapy needed to complete the course. We selected our duration of therapy based on timing of intolerance and difficulties liberating the patient from mechanical ventilation. Ultimately, we chose 6 days (corrected errors on timeline) as this completed a full 21-day course for PJP and the patient had clinically improved at the end of the 21 days.

Changes to the text: See last paragraph of discussion section, page 11 lines 5-17 and discussion about Huang et al on page 10, lines 1-14.

Reviewer B

Interesting case report about usage of echinocandin during P. jirovecii pneumonia. Maybe the text is little bit too long, but the English syntax is quite good. Before

potential acceptance for publication, please address the following gaps:

Comment 1: - Please write scientific names with Italic font and with a capital letter at the genus.
Response 1: We thank the reviewer for this suggestion, and we have fixed throughout the paper.
Changes to text: See track changes throughout.

Comment 2: - Specify how many cycles where needed for qPCR to be determined as positive. By the way, was microscopic observation carried out?
Response 2: We thank the reviewer for this suggestion. The PCR was positive on the first test from the BAL on day 5 of admission. This was the first time it was tested. There were no other microscopic observations carried out besides the positive PCR and the positive BD-Glucan. In terms of microbiology cycles for qPCR (denaturation, annealing, extension) the had to be run in order to reach the threshold of positivity, unfortunately we do not have access to this information. Our microbiology lab does not report this information in the medical record.
Changes to the text: There were no changes to the text made.

Comment 3: - l.76, specify how are graded alternative treatments according to international guidelines?
Response 3: We thank the reviewer for this suggestion. We have updated the introduction paragraph to give graded preference for alternative agents in moderate and severe disease.
Changes to text: See page 5, lines 19-22

Comment 4:- Some case reports and series are actually lacking in Table 1, e.g. Beltz K et al 2006, Zhang J chuan et al 2006, Annaloro C et al 2006, Lee N et al 2017, Ceballos ME et al 2011 ...
- add the following references to advocate more the usage of echinocandin in such a context: PMID: 37321395 and PMID: 32194238
Response 4: We thank the reviewer for this suggestion. We intentionally did not use Beltz within our table as this was a pediatric patient and dosing varies for these medications between adults and children. We have added the word “adult” to Table 2 for clarity. Zhang et al was left out as the only paper available was in Chinese, therefore we could not discern pertinent information for our table. We intentionally did not include Annaloro C et al 2006 as the patient completed a full course of TMP/SMX. When the patient returned, a suspected recurrent episode of PJP was not detected on microscopy, and the authors note that the patient may have had a different fungal infection that was responsive to caspofungin. We also intentionally did not include the papers by Lee et al 2017 and Ceballos ME et al 2011 as we focused our table only on non-HIV patients with PJP to describe patients similar to our case. Both of these case reports report use of echinocandin therapy in HIV patients. We have included “HIV-negative” to this table for clarity. We have added the requested

references to advocate for echinocandin usage.
Changes to text: Added requested references (reference 7 and 8).