



SDI Review Form 1.6

Journal Name:	Journal of Advances in Medical and Pharmaceutical Sciences
Manuscript Number:	Ms_JAMPS_49029
Title of the Manuscript:	USE OF MICA FUNGIN FOR THE MANAGEMENT OF A CLUSTER OF INVASIVE ASPERGILLOSIS IN CHILDREN WITH CANCER
Type of the Article	

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound. To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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SDI Review Form 1.6

PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments		
Minor REVISION comments	<p>Abstract</p> <ol style="list-style-type: none"> Cure for cancer is 100% beneficial, how this would create an unmet need is not clear. Is invasive fungal infection really an unmet need? Key words – should be written in italics, and outbreak should be excluded. <p>Introduction</p> <ol style="list-style-type: none"> Too long, if it is reduced to 3 pages, it could flow better. 'Clusters of IFI have been repeatedly reported also in pediatric patients' – please remove this statement because it has been repeated in the previous paragraph The statement below needs a reference <p>Micafungin (50 mg) has been compared with itraconazole (5 mg/kg) for the prophylaxis of invasive fungal infections in HSCT recipients in a randomized, multicenter, open-label, non-inferiority trial.</p> <ol style="list-style-type: none"> The statement below is not clear – an alternative is preferred. <p>The rates of proven or probable (but not possible)</p> <p>Methodology</p> <ol style="list-style-type: none"> With respect to the statement below, does it imply that only cancer patients are treated in this children's hospital? <p><i>Patients and definition.</i> During a four-month time interval (December to April), all patients admitted in the ward received prophylaxis during the entire hospitalization if they had severe neutropenia (<500/mm³) regardless of the underlying disease. 27 children enrolled for the study, and all had prophylaxis for invasive aspergillosis. How then did you make a diagnosis of disease outbreak, when no one was infected? I don't think there was outbreak during the study period. The study was on children, but the age range was 2 months – 21 years. 18 years and above are adults. Obviously the paediatric disposition of this study is in doubt. </p>	<p>We apologize for the unclear statement, which has been modified as follows: "Progressive increase of the capacity to cure children with cancer makes their rescue from life-threatening, treatment-associated infectious complications, including invasive fungal infections, a compelling challenge". We hope this makes it more clear the point This was modified as suggested</p> <p>This was modified as suggested, to less than 3 pages.</p> <p>This was modified as suggested</p> <p>Citation of Ref. N. 29 has been introduced after this sentence</p> <p>The results in the two arms were not different, as stated above. Thus, this statement, potentially confusing, was simply omitted</p> <p>Although Meyer children hospital treats children with any disorder, the study was conducted in the Hematology-Oncology ward, where the cluster of IFI had been observed and only children with cancer (or congenital immune deficiency) are treated.</p> <p>We apologize for being not fully clear. The outbreak had been observed in the preceding time interval, as stated in the last paragraph of the introduction: "Over a three-month time interval, during fall (October to December), we recorded in our pediatric hematology-oncology ward a total of 14 cases of IA; 4 were possible and 10 probable, according to the guidelines of the European Organization for Research and Treatment of Cancer/Mycoses Study Group.[29] (...) This number of events compared unfavorably with the historical control of about two cases of IFI per year in the patient population on treatment in our ward during the previous five years. Thus, it strongly suggested the occurrence of an outbreak (...)". To be more clear, we introduced the following statement at the end of introduction "In this paper, we describe the results of this program, aimed at breaking the observed cluster of</p>



SDI Review Form 1.6

	<p><u>Discussion</u></p> <ol style="list-style-type: none">1. The characteristics of the patients admitted and treated during the study period were not different from those of the patients from those of the 14 patients. - Those of the patients is repeated, please delete one.2. The 14 patients who had developed IA in the preceding months are not included in your methodology or results. It's not appropriate to include it in your discussion.3. The pattern of the discussion suggests that the author could not find similar studies in literature. Yet there were no recommendations. What do you recommend? <p><u>Conclusion</u></p> <ol style="list-style-type: none">1. The conclusion is not focused – it contains elements that should be in the discussion, such as the statements below: <p>‘Our neutropenic patients, exposed to an obvious environmental risk, were allowed to carry on their therapeutic program without any reduction of the dose-intensity. The i.v. route of administration allowed reaching protective blood levels within a very short time,</p>	<p>IFI by prevention of further cases of IFI in our ward.”</p> <p>Of the 27 patients, one (who had recently admitted, for a previous chemotherapy cycle, during the observed outbreak of IA), was diagnosed with IA on day 2, and thus considered as breakthrough. This was mentioned in the results section, at the study population paragraph.</p> <p>In our hospital, children with cancer are admitted when diagnosed at an age of 18 years or younger, with the only exception of adolescents with bone tumor, who are allowed to be admitted when up to 21 years. This is due to a special competence on this topic developed in our center. In this study, only two patients were older than 18 years (21 and 19 years). Thus, in our opinion this remains indeed a largely pediatric study.</p> <p>We apologize, this was done</p> <p>This statement was omitted.</p> <p>Indeed, we decided to be very cautious in expressing recommendation. We only exposed in the discussion what we considered the “pros” of our experience, but also the limitations of the study. In the conclusion, we state “Our choice of prophylaxis with micafungin, although its use was off-label, turned out to be safe, feasible and very effective in apparently breaking (or at least being associated with break of) the cluster of IA in our ward.” This is a clear endorsement of our experience, although we leave to the readers the opportunity to adopt this approach in future situations</p> <p>This was modified as suggested. The paragraph is now shorter and more focused</p> <p>This reference was omitted and the remaining were re-numbered in the text</p>
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	and the nurses considered the single daily dose convenient' <u>Reference</u> 1. Reference number 14 was not sighted, please include it.	
<u>Optional/General</u> comments		

PART 2:

	Reviewer's comment	Author's comment <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Are there ethical issues in this manuscript?	<i>(If yes, Kindly please write down the ethical issues here in details)</i>	