Reviewer's report

Title: Systematic review and mixed treatment comparison of randomized clinical trials of primary oral antifungal prophylaxis in allogeneic hematopoietic cell transplant recipients

Version: 2
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Reviewer: Peg Carver

Reviewer's report:

This manuscript provides a meta-analysis of antifungal prophylaxis in allogeneic hematopoietic cell transplant recipients. I will note that I am not an expert in meta-analyses and thus cannot comment on the methodology utilized for that analysis. While an interesting analysis, the authors included very few studies as the basis for their analysis. The rationale for inclusion or exclusion of studies was poorly defined (with the exception of the explanation provided for the Slavin study), and further clarification is required prior to recommending publication of this manuscript.

Although a discussion of the results of a 2007 meta-analysis was included, a (more) recent meta-analysis by Ziakis et al1 was not presented. Comparison of the Ziakis and Robenshtok studies’ methodology and results to that of the current analysis would be beneficial. Similar to the Robenshtok analysis, these authors concluded that there was comparable effectiveness of antifungal drugs, while acknowledging the paucity of comparable studies for newer, possibly more effective agents such as micafungin, voriconazole, and posaconazole. I disagree with excluding the Slavin fluconazole vs placebo study (ref 26). The fact that neither arm had mold coverage is important in evaluating the overall efficacy (or lack thereof) of various antifungal regimens. While the reference is ‘old’, and would likely underestimate the incidence of mold infections, it would still be of value to include while noting that caveat. How was ‘old’ defined/determined?

The authors appear to have confined their analysis to trials which included ONLY alloHSCT patients, and and thus, excluded a number of trials2-13 (including the excluded Slavin study3) which included both allo and auto transplant patients. (Several of these2, 3, 7, 8 are ‘older’ studies if 1995 is the ‘cutoff’ for being too old.) I recognize that patient level data may not be readily available from these trials; however, excluding them is an important difference in this study vs previous meta-analyses, and the decision defending this should be discussed. It should be noted, however, that a newer (2012) study by Chaftari et al which compared posaconazole and weekly ABLC that included only alloHSCT which was not included (or mentioned).14 The relative ‘risk’ of HSCT patients differs greatly if they have GVHD; however, many studies do not include this level of detail in their publications, making comparisons between studies difficult.

1. Ziakas PD, Kourbeti IS, Mylonakis E. Systemic Antifungal Prophylaxis After


**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

competing interests:
1. Previous grant support from Merck and Astellas
2. Member of speakers bureau (Merck and Astellas)