Reply to “What Types of Candida Infections Should Be Included When Evaluating Breakthrough Infections during Posaconazole Prophylaxis?”

Michael J. Dolton,* Andrew J. McLachlan*a,b
Faculty of Pharmacy, University of Sydney, Sydney, Australia; Centre for Education and Research on Ageing, Concord Repatriation General Hospital, Sydney, Australia

We thank Dr. Blennow and Dr. Kalin for their comments (1) relating to our recent paper (2). They argue that some of the cases included in our study as breakthrough fungal infections occurring while patients were taking posaconazole prophylaxis are not cases of “invasive” fungal infections (IFIs).

To clarify, we agree that case 4 (culture-proven oral candidiasis), case 7 (culture-proven urinary tract infection), and case 8 (presumed fungal endophthalmitis) do not meet the criteria of an IFI (3); however, in our paper we do not claim this to be the case. It is important to note that our study investigated the exposure-response relationship for posaconazole prophylactic efficacy in preventing breakthrough fungal infections, including, but not limited to, IFIs. Clinically, the development of these breakthrough fungal infections while patients were taking posaconazole was treated as a failure of posaconazole prophylaxis, prompting treatment of the breakthrough infection with an alternative antifungal agent(s) (with the exception of case 4, where follow-up was not documented in the medical record).

Furthermore, a reanalysis of our data by examining only patients meeting the definition of a breakthrough IFI does not alter the conclusion that there is a significant exposure-response relationship between posaconazole plasma concentrations and prophylactic efficacy arising from the study. When the cases disputed by Blennow and Kalin are instead included as patients who did not develop a breakthrough fungal infection, patients who developed a breakthrough IFI had significantly lower posaconazole concentrations than those who did not develop a breakthrough IFI (median, 315 ng/ml versus 469 ng/ml; P < 0.05), mirroring our original analysis and conclusions.

Blennow and Kalin also mention that seven of the cases of breakthrough fungal infection met the criteria of a possible IFI. As discussed in our paper, galactomannan and β-D-glucan tests were not widely available in the hospitals included in this study. Had these tests been available, it is possible that a number of these cases of possible IFI would have met the criteria of probable IFIs.

REFERENCES

Address correspondence to Andrew J. McLachlan, andrew.mclachlan@sydney.edu.au.