antifungal agents; the study was not powered for such comparisons. In the full analysis set at end of prophylaxis (Table 2 in our study), the number and rate of IFIs was 4 of 172 treated patients (2.3%) for micafungin, 1 of 23 (4.3%) for caspofungin, 4 of 71 (5.6%) for liposomal amphotericin B, and 3 of 78 (3.8%) for fluconazole. As Winston and colleagues mention, TENPIN’s results are in line with those of Sun et al [1]. However, theirs was a retrospective analysis comparing micafungin and amphotericin B in a limited patient number who received different antifungal prophylaxis in sequential time periods, not allowing a firm conclusion on the comparative efficacy of the 2 strategies. Conversely, TENPIN was randomized, multicenter, and prospective, utilizing a large study population.

Evidence suggests that widespread fluconazole use has contributed to changes in the epidemiology of invasive candidiasis. Prevalence of non-albicans Candida species that exhibit reduced fluconazole susceptibility has increased [2, 3], including C. glabrata, the most common non-albicans Candida species among solid organ transplant recipients [4]. Therefore, the 16-year-old fluconazole trial [5] is not as relevant today. Interestingly, all 9 isolates tested in the Winston et al study were susceptible to anidulafungin, whereas 5 of 8 (63%) were fluconazole resistant [6].

Comparisons between TENPIN and Winston et al [6] are more relevant. However, as the Winston et al study was powered for superiority and did not meet its primary endpoint, no firm conclusions are reached. We concur that with the lower IFI incidence in patients treated today, it would be difficult to demonstrate any drug’s superiority without recourse to an impractically large study population. We noted the potential difference in favor of anidulafungin in Aspergillus colonization, IFI risk in certain subgroups, and breakthrough IFI incidence among patients who had received pre-transplant fluconazole. Also, fluconazole significantly affected tacrolimus levels in their study, which has potentially important clinical implications for the transplanted organ and patient management.

Our respective studies demonstrate the value of antifungal prophylaxis in high-risk liver transplant patients and suggest that echinocandins are at least as effective as standard of care. We agree that each transplant center should adopt a prophylaxis strategy based on local conditions and individual patients, which is why each TENPIN center specified its own standard of care. Regimen choice is governed by several factors, including prevailing azole resistance rates, regional variation, and patient population risk factors. Considering the impact of an IFI on graft and patient survival [7], we choose echinocandins for prophylaxis to circumvent such difficulties as differentiating between risk factors for aspergillosis and candidiasis, identifying colonizing species with reduced susceptibility or resistance to azoles, and potential drug-drug interactions between fluconazole and tacrolimus.

Notes

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