Safety and Efficacy of Itraconazole Compared to Amphotericin B as Empirical Antifungal Therapy for Neutropenic Fever in Patients with Haematological Malignancy*

Abstract:
Safety, tolerability and efficacy of itraconazole and amphotericin B (AMB) were compared for empirical antifungal treatment of febrile neutropenic cancer patients. Patients and Methods: In an open, randomised study, 162 patients with at least 72 h of antimicrobial treatment received either intravenous followed by oral itraconazole suspension or intravenous AMB for a maximum of 28 days. Permanent discontinuation of study medication due to any adverse event was the primary safety parameter. Efficacy parameters included response and success rate for both treatment groups. Results: Significantly fewer itraconazole patients discontinued treatment due to any adverse event (22.2 vs. 56.8% AMB; p < 0.0001). The main reason for discontinuation was a rise in serum creatinine (1.2% itraconazole vs. 23.5% AMB). Renal toxicity was significantly higher and more drug-related adverse events occurred in the AMB group. Intention-to-treat (ITT) analysis showed favourable efficacy for itraconazole: response and success rate were both significantly higher than for AMB (61.7 vs. 42% and 70.4 vs. 49.3%, both p < 0.0001). Treatment failure was markedly
reduced in itraconazole patients (25.9 vs. 43.2%), largely due to the better tolerability. Conclusions: Itraconazole was tolerated significantly better than conventional AMB and also showed advantages regarding efficacy. This study confirms the role of itraconazole as a useful and safe agent in empirical antifungal therapy of febrile neutropenic cancer patients.