
ELIMINATION OF ASPERGILLUS AS A SIGNIFICANT PATHOGEN IN AN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT PROGRAM AFTER INTRODUCTION OF ROUTINE LONG-TERM ITRACONAZOLE PROPHYLAXIS.

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Invasive fungal infections are a common cause of morbidity and mortality in allogeneic hematopoietic stem cell transplant (HSCT) recipients. At many transplant centers, *Aspergillus* is the leading cause of death from fungal infection. In a prospective randomized trial, we found itraconazole was more effective than fluconazole for long-term prophylaxis of invasive yeast and mould infections after allogeneic HSCT (9% vs 25%, $p=0.01$). Based upon these results, we introduced long-term itraconazole as routine antifungal prophylaxis in all adult patients undergoing allogeneic HSCT at UCLA. Intravenous (IV) itraconazole (200 mg IV q12hrs for 2 days followed by 200 mg IV q24 hrs) was started on day +1 after HSCT and continued until time of engraftment. After engraftment, patients received oral itraconazole solution (200 mg po q12hrs) until day +100. After day +100, oral itraconazole solution was continued in patients still requiring corticosteroids for prevention or treatment of graft-versus-host disease (GVHD). Both in-patients as well as outpatients unable to take oral therapy were returned to IV itraconazole. From December 2001 to December 2003, 73 allogeneic HSCT patients received routine long-term itraconazole prophylaxis. These patients were at high-risk for *Aspergillus* infection (median age 40yrs, range 18-64 years; advanced disease 78%; previous HSCT 20%; unrelated donor 41%; high-dose corticosteroids for prevention or treatment of GVHD 84%; grade 2-4 GVHD 46%). None of the 73 patients developed *Aspergillus* infection, which is significantly lower than the incidence of *Aspergillus* infection in similar matched UCLA allogeneic HSCT patients receiving fluconazole prophylaxis before December 2001 (0% vs 13%, $p=0.004$). Two cases of candidemia caused by itraconazole-sensitive organisms (*C. albicans* and *C. tropicalis*) were the only invasive fungal infections. Overall survival was 59%, but no deaths were related to fungal infection. Except for nausea and vomiting (18% incidence), itraconazole was well-tolerated. These results suggest that invasive *Aspergillus* infections can now be successfully prevented in high-risk allogeneic HSCT patients by routine long-term prophylaxis with an azole agent like itraconazole active against moulds.