

**[163] Results of a Randomized, Double-Blind Trial of Fluconazole (FLU) vs. Voriconazole (VORI) for the Prevention of Invasive Fungal Infections (IFI) in 600 Allogeneic Blood and Marrow Transplant (BMT) Patients. Session Type: Oral Session**

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A multi-center, randomized, double blind trial was performed to determine the impact of FLU (400 mg daily in adults) vs. VORI (200 mg twice daily in adults) on the prevention of IFIs in standard risk allogeneic BMT patients receiving full-intensity conditioning regimens. 600 patients with AML (n=230), ALL (n=122), CML (n=103), MDS (n=98), lymphoma (n=43) and other diseases (n=4) were randomized; 295 to FLU, 305 to VORI between 2003 and 2006 (1 not transplanted). Study drugs were given for 100 days; in those receiving prednisone at a dose of  $\geq 1$  mg/kg/day at day 100 or for recipients of T cell depleted grafts with CD4+ counts  $< 200$  at day 100, drugs were administered for 180 days. All patients had serum galactomannan (GM) assayed twice weekly for 60 days, then once to twice weekly until day 100, depending on severity of graft versus host disease (GVHD). Positive GM, radiology or the presence of suspicious symptoms or signs triggered intensive evaluation for IFI. Empirical antifungal therapy was permitted for suspected IFI during diagnostic assessment but was limited to  $\leq 14$  days. The primary endpoint was freedom from IFI or death at 6 months (fungal-free survival) in the intent to treat cohort. Median recipient age was 43 years (range, 3-66) with 92%  $> 18$  years; 55% male; 95% with HLA A, B, and DRB1 matched donor; stem cell graft was related donor marrow or PBSC in 56%. There were no significant differences between the two arms in patient, disease type or risk, or transplant characteristics. Rates of engraftment, acute or chronic GVHD, non-fungal infections, expected or unexpected severe adverse events, and rates of premature study drug withdrawal were similar in both arms (p=NS). At a median follow-up of 12 months, overall survival was 80% at 6 months and 67% at 12 months. A blinded data review committee reviewed source documents of all reported fungal infections, deaths, patients with a positive GM and those given empirical antifungal therapy. There were 25 proven, 30 probable, 15 presumptive, and 74 possible IFIs. The cumulative rates of proven, probable and presumptive IFI were similar in the two arms: 10.6% for FLU and 6.6% for VORI at 6 months (p=0.11) and 13.1% and 11.6% at 12 months (p=0.50), respectively. Microbiologically documented IFIs at 6 months in each arm (FLU and VORI) were caused by *Aspergillus* (16 and 7, p=0.05), *Candida* (3 and 3), *Zygomycetes* (3 and 2), and other (1 and 1). Fungal-free survival rates were similar: 76% for FLU and 78% for VORI at 6 months (p=NS) and 65% and 63% at 12 months (p=NS), respectively. Event-free and overall survival rates also were similar in both arms at 6 and 12 months (p=NS). There were no differences in fungal-free survival rates in patients who received prophylactic fluconazole or voriconazole when intensive monitoring and early empirical therapy were employed in standard risk allogeneic BMT recipients.