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POST MARKETING SURVEILLANCE OF VORICONAZOLE (VORI) USE IN HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) RECIPIENTS AT A SINGLE ACADEMIC INSTITUTION

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VORI, a second generation triazole, was approved by the FDA on 5/28/02. One of the major concerns with VORI is its adverse drug reaction profile and the numerous drug interactions that are likely to occur in pts receiving polypharmacy. We retrospectively evaluated all pts receiving VORI admitted to the HSCT program from 08/02 - 10/20/03. Of 45 evaluable pts, 11% underwent autologous HSCT, 22% allogeneic HSCT, 20% MUD HSCT, 7% UCB, and 40% received chemotherapy for leukemia or lymphoma. Twenty pts (44.5%) received steroids prior to VORI (7 received <1 mg/kg/d; 5 x 1 mg/kg/d; 1 x 1.5 mg/kg/d and 7 x 2 mg/kg/d). VORI was was used empirically in 76% of cases, prophylactically in 9%, and was used to treat documented fungal disease in 15%. According to the EORTC/MSG definitions for IFI, 29% of pts had a proven infection, 56% had a possible IFI, and 6% did not meet established criteria. VORI was used as first-line therapy in 82% pts. Of the documented infections treated, there were 2 *Aspergillus* non-*fumigatus*, 2 *A.fumigatus*, 1 *A. flavus*, 2 *Fusarium* spp., 1 Basidiomycete, 1 *Curvularia* spp., 1 dematiaceous mold, 1 *Candida albicans*, and 1 polyfungal infection (*A. fumigatus* and *Penicillium* spp.). CR's were seen in 15% cases, PR's in 46% cases and PD occurred in 38% cases. Combination therapy was used in 20% of pts (5 VORI + caspofungin; 2 VORI + ABLC, 1 VORI + cAmB, 1 VORI + AmBisome, 1 VORI + AmBisome + caspofungin).

Mean duration of voriconazole was 27 days (range 2 - 130). Loading doses were administered in 87% pts. VORI was administered PO in 76% pts and 22% IV, 2% PO + IV. Interacting medications were prescribed in 87% pts. The interaction of greatest concern is between calcineurin inhibitors (CyA and FK506) and VORI. Calcineurin inhibitors were prescribed to 20 pts (44%). Of these, 13 (65%) were succesfully dose adjusted to achieve therapeutic serum concentrations, 5 (25%) had dose modifications, but resulted in supratherapeutic concentrations, and 2 pts did not have the required dose modification made (1 resulting in toxicity). Adverse events were seen in 15 pts (3 visual;1 AMS; 11 abnormal LFT's). Of pts with normal BL LFT's, 15% had increases in bilirubin, 28% in AST, 15% in ALT, and 28% in alk phosphatase.

Among the documented infections treated, VORI resulted in similar response rates to published studies. It is effective, and while there are numerous drug interactions, if managed appropriately, this is a safe agent to use in this high-risk population.

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PILOT STUDY OF ORAL DOLASETRON AND DEXAMETHASONE FOR THE CONTROL OF NAUSEA AND VOMITING ASSOCIATED WITH HIGH-DOSE CHEMOTHERAPY FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION

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The efficacy of oral dolasetron and dexamethasone in patients receiving high-dose chemotherapy followed by autologous stem cell transplantation was evaluated. In an open-label, non-comparative study, 43 patients who received conditioning with high-dose chemotherapy were given oral dolasetron 100 mg daily (one hour prior to each dose of chemotherapy) and on each day of rest. Patients also received oral dexamethasone 10 mg twice daily, starting one hour prior to the first dose of chemotherapy and continuing through each day of rest. Patients were permitted to use prochlorperazine, lorazepam, haloperidol, and/or droperidol on an as-needed basis at their request. Objective data such as number of emetic episodes and quantity of rescue medications used during the study period were recorded. Subjective rankings of nausea and vomiting were assessed using a 100 mm visual analogue scale every 12 hours throughout the study period. The overall response rate was 85% (67.5% complete response, 17.5% partial response). The mean number of emetic episodes was <0.2 on each day of the study, and a mean of <2 rescue medications were used each day. Mean visual analogue scores did not exceed 25 mm at any time during the study. No unexplained laboratory or clinical parameters were noted. The data suggest that the combination of oral dolasetron and oral dexamethasone is safe and effective in controlling nausea and vomiting in patients undergoing high-dose chemotherapy followed by autologous stem cell transplantation.

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TWICE DAILY CEFEPIME FOR FEBRILE NEUTROPENIA FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANTATION

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Neutropenic patients following high-dose chemoradiotherapy and autologous hematopoietic stem cell transplantation (HSCT) are predisposed to potentially life-threatening infections. Cefepime two grams every eight hours is an established monotherapy regimen. Cefepime two grams twice daily is efficacious for numerous other indications and would be a convenient alternative for HSCT inpatients and outpatients.

Following IRB-approval, a retrospective, single institution cohort study of 171 autologous HSCT patients was conducted. From 1998 to 2000, 88 females and 83 males received cefepime twice daily for neutropenic fever. Median age was 54 years (range, 20-76) and underlying diagnoses included lymphoma (n = 67), myeloma (n = 48), solid tumor (n = 25), amyloidosis (n = 17), leukemia (n = 12), and scleroderma (n = 2). Cefepime was initiated between day +2 and +17 (median, +6) following HSCT. Duration of therapy ranged from 1 to 20 days (median, 6).

Immunocompromised Host Society outcome criteria were strictly applied. A failure was ascribed if any antimicrobial was added secondary to persistent fever or culture results within 72 hours of initiation. Forty-two patients (24.5%) successfully eradicated neutropenic fever or microbiologically documented infection. Seventy patients (40.9%) developed positive blood cultures; 12 of 70 (17.1%) were polymicrobial. Forty-one patients (58.6% of all bacteremias) were coagulase negative Staphylococci (SCN) while gram-negative bacilli occurred in 18 (25.7%). Twelve patients (7%) received empiric antifungal therapy and one patient died (0.6%) secondary to infection (aspergillosis). Time to defervescence ranged from 1 to 20 days (median, 5) while neutropenia lasted 4 to 106 days (median, 9). Forty-seven patients (27.5%) initially responded, but had modification to their regimen when secondary infections arose [e.g. Clostridium difficile (n = 15)], or adverse effects developed [e.g. rash (n = 22)]. Overall, eighty-nine patients (52%) initially responded. Eighty-two patients (48%) were classified as failures. Frequent SCN bacteremias and infections outside the spectrum may partially explain the failure rate. Twice daily cefepime is convenient, effective therapy, but frequently requires modification.