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TWICE-WEEKLY ABLC PROPHYLAXIS FOR PATIENTS AT HIGH RISK OF INVASIVE FUNGAL INFECTION AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Invasive fungal infections (IFIs) are increasing after allogeneic stem cell transplantation (aSCT). Known prognostic factors for IFI include mismatched donors, severe GvHD, CMV infection, and the use of steroids. Our group treated all patients during their initial neutropenic episode with oral fluconazole or itraconazole (200–400 mg/day). Starting on day +30, patients who received prednisone ≥ 30 mg/day were switched to intravenous amphotericin-B lipid complex (ABLC; Abelcet) at a dosage of 4 mg/kg twice a week. Patients who received lower steroid doses continued their fluconazole/itraconazole until at least day +100 after SCT. Between 1999 and 2002, a total of 100 patients were enrolled, including 24 patients with unrelated donors and 11 patients with partially mismatched related donors. Good-risk patients were a minority (27%), whereas 32% had overt relapse and/or refractory disease. Preparative regimens contained TBI (45%), busulfan/cyclophosphamide (35%), or fludarabine (20%). BM and PBSC were the source of stem cells in 43% and 57% of patients, respectively. Prophylaxis of aGvHD was based on cyclosporine but included steroids in 27%, in vivo T-cell depletion in 25%, and in vitro T-cell depletion in 15% of patients. Out of 37 patients who did not receive ABLC prophylaxis, 2 developed IFI beyond day +30 (1 from *Aspergillus* on day +36, 1 from *Candida* on day +63). A total of 63 patients did receive prophylactic ABLC for a median of 52 days (range, 1 to 289 days). Six of the patients at such high risk of IFI that they were assigned to ABLC prophylaxis still developed IFI (3 from *Aspergillus* at days +45, +65, and +255 and 3 from *Candida* at days +70, +72, and +210). An additional 2 patients had probable, but undocumented, IFI. Univariate analysis of all patients with IFI showed that factors increasing the risk of IFI were BM as the stem cell source, MUD or PMRD, severe GvHD, and CMV infection ($P < .01$ in all comparisons). Interestingly, the use of steroids (and/or use of ABLC) was no longer a prognostic parameter. The twice-weekly ABLC was well tolerated, with a median increase in creatinine of 0.85 mg/dL.

This regimen of twice-weekly intravenous ABLC 4 mg/kg appears to compensate for the increased risk of IFI associated with the use of steroids after allogeneic SCT. This prophylaxis resulted in a low incidence of IFI in this analysis of 100 allograft recipients and allowed the use of higher doses of steroids. To increase its early efficacy, the twice-weekly ABLC prophylaxis perhaps should be started earlier than day +30.

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AMD3100 PLUS G-CSF RAPIDLY MOBILIZES HEMATOPOIETIC PROGENITOR CELLS IN PATIENTS WITH NON-HODGKIN'S LYMPHOMA (NHL) AND MULTIPLE MYELOMA (MM), INCLUDING THOSE TRADITIONALLY CONSIDERED "POOR MOBILIZERS"

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AMD3100 is a potent, selective antagonist of the CXCR4 chemokine receptor, blocking binding of its cognate ligand, stromal cell–derived factor 1α. Administration leads to elevations in circulating hematopoietic progenitor cells after 10–11 hours. Preliminary studies showed that more progenitor cells were mobilized into the circulation when G-CSF and AMD 3100 were administered to patients compared to G-CSF administration alone. To investigate the degree of progenitor cell mobilization of AMD3100 and G-CSF (10 μg/kg/day), we treated unselected patients undergoing autotransplantation for NHL and MM. G-CSF at 10 μg/kg/day for up to 9 days was administered SQ with AMD3100 at 240 μg/kg/day SQ starting on the evening of day 4 of G-CSF (10–11 hours before planned daily aphereses) until 5×10^6 CD34/kg were collected, or to a maximum of 5 days of a standard 3 blood volume apheresis. Of 43 patients entered to date, 20 (6 myeloma, 14 NHL) have been analyzed. Of these 20, 14 are considered to have been heavily pretreated using standard definitions (10 cycles of chemotherapy, platinum-based salvage chemotherapy, and/or radiation therapy to bone marrow sites).

Blood CD34 assays (cells/μL) were performed before and after each AMD 3100 dose and on each apheresis product. After the first dose of AMD3100 there were 2.6-fold and 3.0-fold increases in CD34 cells/μL in blood for the NHL and MM patients, respectively. A median 2 aphereses were performed (range, 1–5); the median total CD34 collected was 5.7×10^6/kg (range, 2.32–14.58×10^6/kg). All patients had collections of $> 2.0 \times 10^6$ CD34 cells/kg, and in 14, the 5×10^6 CD34/kg cell dose goal was collected, including 8 of 14 in the heavily pretreated group. In 6 patients, the 5×10^6 CD34/kg cell dose was collected in a single apheresis. The median CD34/kg cell dose collected for the 14 heavily pretreated patients was 6.0×10^6/kg.

There were no serious adverse eeffects related to the use of AMD3100. Transient diarrhea occurred in 44% shortly after the injections of AMD3100, but only 3 patients required therapy. Engraftment data for the first 12 patients treated demonstrated time to ANC > 500/μL and platelets > 20,000/μL of 9 days (range, 8–10) and 12 days (range, 9–19), respectively.

The combination of AMD3100 and G-CSF appears to be effective in mobilizing large numbers of CD34+ cells, and appears superior to G-CSF alone in heavily pretreated patients, in whom it appears to be a potentially less-toxic alternative to chemotherapy/cytokine mobilization.

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INFLUENCE OF IMMUNOSUPPRESSIVE AGENTS ON MAGNESIUM (MG) METABOLISM AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): COMPARISON BETWEEN CYCLOSPORINE A (CSA) AND TACROLIMUS

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Background: Calcineurin inhibitors, CSA and tacrolimus, are universally used for the prophylaxis and treatement of graft-versus-host disease (GVHD) after allogeneic HSCT. In addition to their common adverse effects, including renal dysfunction, CSA and tacrolimus cause hypomagnesemia due to the suppression of reabsorption of Mg from renal tubules. Because hypomagnesemia has reportedly been associated with renal dysfunction and encephalopathy by CSA and tacrolimus, strict monitoring and management of serum Mg level are necessary. We performed a prospective study to evaluate Mg metabolism in recipients of allogeneic HSCT who were receiving CSA or tacrolimus. **Methods:** Consecutive patients undergoing allogeneic HSCT at Keio University Hospital between January 2003 and July 2004 were enrolled. CSA (3 mg/kg/day) and tacrolimus (0.03 mg/kg/day) were administered intravenously by continuous infusion starting from day −1. The doses were arranged to maintain blood levels at 200–400 ng/mL for CSA and at 15–20 ng/mL for tacrolimus. Serum Mg and the total amount of daily Mg excretion in urine were measured once before the administration of CSA or tacrolimus, and then once weekly after HSCT for 4 weeks. Mg was supplemented intravenously by continuous infusion to maintain the serum Mg level > 1.5 mEq/L. **Results:** Thirty-six patients were evaluable (12 in the CSA group and 24 in the tacrolimus group). The serum Mg level began to decrease in both groups from the first week after HSCT, and was significantly lower in the tacrolimus group than in the CSA group from the first to the third weeks ($P < .01$). The total amount of daily Mg excretion in urine and Mg supplementation began to increase in both groups from the second week after HSCT, and they were significantly higher in the tacrolimus group than in the CSA group ($P < .01$). **Conclusions:** Although both CSA and tacrolimus in-