LONG-TERM FOLLOW-UP OF 103 PATIENTS WHO RECEIVED RECOMBINANT HUMAN GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR AFTER UNRELATED DONOR BONE MARROW TRANSPLANTATION

To the Editor:

Previously we reported results of 40 patients who received recombinant human granulocyte-macrophage colony-stimulating factor (rhGM-CSF) after unrelated donor bone marrow transplantation (BMT).1 We now report long-term follow-up of the initial 40 patients and 63 consecutive additional patients studied between 10/25/90 to 9/6/91 who received rhGM-CSF after unrelated donor BMT. All patients entered into the trial received cyclophosphamide (60 mg/kg × 2) and total body irradiation (1,000 to 1,320 cGy) before receiving HLA-matched (n = 79) or one antigen minor mismatched (n = 24) unrelated donor marrow. The median total nucleated cell dose of infused marrow was $2.9 \times 10^9$ cells/kg. Cyclosporine and methotrexate (on days 1, 3, 6, and 11) were administered to all patients for graft-versus-host disease (GVHD) prophylaxis. The median patient age was 30 years. Seventeen patients had acute and 61 had chronic myeloid leukemia; 19 had acute lymphocytic leukemia, 3 had lymphoma, and 3 had aplastic anemia. rhGM-CSF (250 µg/m²/d; ImmuneX corp, Seattle, WA) was administered from day 0 to 20 (n = 11) or 27 (n = 92) by 2-hour infusion. Toxicity attributed to rhGM-CSF was minimal. rhGM-CSF was discontinued early in 4 patients for infection, 3 for veno-occlusive disease, 5 for early neutrophil recovery, 1 for graft delay, 1 with the recurrent disease, 4 with pericarditis, and 1 for a skin rash. Two patients developed graft failures; one failed to engraft and another had secondary graft loss. Within the first 100 days, 42 patients developed grade II GVHD, 39 developed grade III GVHD, and 7 developed grade IV GVHD. The median days to achieve an absolute neutrophil count (ANC) to ≥100, 500, and 1,000/mm³ were achieved on days 18, 21, and 23, respectively. The median day of platelet transfusion independence was day 23, and the median number of platelet units transfused within the first 20 days after marrow infusion was 97. The median maximum creatinine and bilirubin over the same time period was 1.4 mg/dL and 5.5 mg/dL, respectively. Sixteen percent of patients had documented bacterial (n = 13) or fungal (n = 4) infections. The median number of days with a temperature ≥38.5°C was 5.

The incidence of GVHD and the rate of neutrophil and platelet recovery were not different than data published from other centers and previously published historical control patients (n = 78) who did not receive rhGM-CSF.2,3 The rate of recurrent disease at 2 years was not different (P = .90). The incidence of infection was slightly less (16% vs 27%) and nonrelapse mortality was less in patients who received rhGM-CSF than in historical control patients (34% vs 51%, P = .02).

In conclusion, administration of rhGM-CSF was not associated with significant long-term adverse effects, particularly with respect to GVHD and graft rejection. The incidence of infection was less and nonrelapse mortality was lower in patients who received rhGM-CSF than in historical patients from the Fred Hutchinson Cancer Research Center. However, prospective randomized placebo-controlled trials are necessary to confirm actual benefit of rhGM-CSF.

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REFERENCES
Long-term follow-up of 103 patients who received recombinant human granulocyte-macrophage colony-stimulating factor after unrelated donor bone marrow transplantation [letter]

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