

Hematologic malignancy risk with granulocyte colony-stimulating factors

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This feature is designed to help protect your patients with updates on adverse events related to various cancer treatments.

Instances have been reported of hematologic malignancies developing in previously healthy peripheral blood stem cell donors who received granulocyte colony-stimulating factor (G-CSF). In a study of 200 healthy donors who underwent G-CSF-mobilized stem cell harvesting procedures for sibling stem cell transplants, two patients developed acute myelogenous leukemia (AML) 4 and 5 years later. After intensive chemotherapy, one patient died, whereas the other remains in complete remission. However, it should be noted that more than 60,000 healthy donors have provided G-CSF-mobilized peripheral blood stem cells, with rare reports of hematologic malignancy later developing in these individuals.¹

Hematologic malignancies have also been reported following the use of G-CSF during breast cancer adjuvant chemotherapy.² For example, of 906 breast cancer patients who received G-CSF concurrent with adjuvant chemotherapy, 64 later developed myelodysplastic syndrome (MDS) or AML.³

Four recent database studies on large numbers of patients noted increased risks of AML/MDS development following G-CSF administration. These databases included patients with breast cancer and persons with nonmalignant conditions

associated with increased risk of hematologic malignancies.

Where reported

In 2006, in an article in the *British Journal of Haematology*, the Research on Adverse Drug Events And Reports (RADAR) project of Northwestern University reported two cases of sibling stem cell donors developing AML after G-CSF administration.² Additionally, Hershman et al reviewed the Surveillance, Epidemiology, and End Results (SEER)-Medicare database to identify individuals who received G-CSF concurrently with adjuvant chemotherapy for breast cancer.³ They found the use of G-CSF to be associated with a doubling in the risk of subsequent AML or MDS, even though the absolute risk remained low.

Recommendations

The safety of administering G-CSF to healthy individuals should be evaluated in long-term studies. These studies should compare rates of hematologic malignancy among G-CSF-mobilized donors at high risk for hematologic malignancy (ie, sibling donors) with those of nondonors. G-CSF should be prescribed with caution to healthy individuals and to those patients receiving adjuvant chemotherapy for breast cancer.

References

1. Filgrastim [package insert]. Thousand Oaks, CA: Amgen Inc; 2006.
2. Bennett CL, Evens AM, Andritsos LA, et al. Haematological malignancies developing in previously healthy individuals who received haematopoietic growth factors: report from the Research on Adverse Drug Events and Reports (RADAR) project. *Br J Haematol* 2006;135:642-650.
3. Hershman D, Neugut AI, Jacobson JS, et al. Acute myeloid leukemia or myelodysplastic syndrome following use of granulocyte colony-stimulating factors during breast cancer adjuvant chemotherapy. *J Natl Cancer Inst* 2007;99:196-205.

Fast Facts

COLONY-STIMULATING FACTORS are glycoproteins that bind to specific cell receptors on hematopoietic cells, stimulating activation and proliferation. Filgrastim (Neupogen) is a recombinant granulocyte colony-stimulating factor (G-CSF), produced from *E. coli*, in which the human gene has been incorporated. Clinical indications include treatment of severe chronic neutropenia and febrile neutropenia related to the use of myelosuppressive agents in the treatment of nonmyeloid malignancies, reduction of time to neutrophil recovery and the duration of fever for patients with acute myeloid leukemia (AML), reduction in the duration of neutropenia following bone marrow transplant, and mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis. G-CSF is often used prophylactically to increase white blood cell counts in patients with cancer and has been administered to healthy platelet donors in an effort to improve platelet yields.^{1,2}