

# CLINICAL APPLICATIONS OF GRANULOCYTE COLONY STIMULATING FACTOR (G-CSF)

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Haematopoietic growth factors control the proliferation, maturation and functional activity of various blood cell lineages.

Those of most clinical interest control cell production in the erythroid and granulocyte-macrophage lineages namely, erythropoietin, (Epo) the colony stimulating factors (G-CSF, GM-CSF, M-CSF and Multi-CSF (IL-3), and IL-6 and stem cell factor (SCF). Of these, G-CSF and GM-CSF have undergone clinical trials.

The granulocyte colony stimulating factors have their major proliferative effects on committed progenitor cells and their maturing progeny. Thus, G-CSF stimulates the formation of maturing granulocytic colonies.

Early studies established the G-CSF causes a rapid, dose-dependent and quickly reversible increase in peripheral blood neutrophil counts after i.v. or s.c. application. More recent studies with G-CSF in cancer patients showed substantial reductions in duration and severity of neutropenia following cytotoxic chemotherapy, followed by decreased rates of infectious complications and reduced need for chemotherapy dose reduction or delay.

Recent randomized, placebo-controlled phase III clinical studies with G-CSF in tumor patients have confirmed the reduction of neutropenia and infectious complications. It was also established that G-CSF effect on myelopoiesis is sustained over multiple cycles of chemotherapy and does not occur at the expense of hematopoiesis in other cell lineages.

Several studies have been carried out to determine if G-CSF also offers benefit to patients who receive myeloablative chemotherapy which requires bone marrow (BM) or peripheral blood progenitor cell (PBPC) support. Studies of the use of G-CSF in patients undergoing autologous bone marrow transplantation for Hodgkin's disease, breast cancer and various lymphoid malignancies demonstrated up to a 10-day reduction in the duration of neutropenia, less antibiotic use, less parenteral nutrition and less time in hospital. The duration of thrombocytopenia has not been significantly reduced by either G-CSF or GM-CSF in most studies.

The tolerability profile of G-CSF is favourable. The most frequent side effect is mild to moderate bone pain which occurs in up to 15% of patients depending on G-CSF dosages, and responds well to analgesics.

Other observations include moderate and reversible serum biochemical abnormalities. There is no evidence that G-CSF causes systemic adverse effects sometimes observed with other biological mediators, namely fever, hypotension, dyspnea, or capillary leak syndrome.

Future development issues with G-CSF include evaluation in a broader range of chemotherapy regimens, and to explore the potential of G-CSF to allow new treatment schedules and higher doses of chemotherapy (does intensification or escalation).