

# ADVANCES IN SUPPORTIVE CARE

Current Developments in Side Effect Management, Palliative Care, and Quality of Life

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## Updated ASCO Recommendations for the Use of White Blood Cell Growth Factors

David C. Dale, MD  
Professor of Medicine  
University of Washington  
Attending Physician  
University of Washington Medical Center

**H&O** When did the American Society of Clinical Oncology begin issuing guidelines on the use of white blood cell growth factors?

**DD** These guidelines were first issued in 1994, shortly after the approval of hematopoietic growth factors for the treatment of patients with cancer. The American Society of Clinical Oncology (ASCO) has updated these guidelines several times—in 1996, 1997, 2000, and 2006. Each update has incorporated new information and understanding about how the hematopoietic growth factors, specifically the white blood cell (WBC) growth factors, or what are often called colony-stimulating factors (CSFs), can be used to reduce the risk of fever and infections in patients undergoing cancer treatment.

**H&O** What are the major changes in the 2006 updated guidelines?

**DD** There are several new features in the updated guidelines, but the major change is that the threshold for the probability of developing febrile neutropenia as an indication for administering CSFs has been lowered. This change refers specifically to granulocyte CSF (G-CSF), as most of the clinical data pertain to this growth factor. The probability threshold has been lowered from 40% to 20%; in other words, the recommendations are for broader use of G-CSF to prevent febrile neutropenia and neutropenia in cancer patients receiving standard-dose chemotherapy.

**H&O** On what data is this change based?

**DD** The change is based primarily on evidence of efficacy. Recent clinical trials in which patients with a lower risk of febrile neutropenia were randomized to receive growth factors or no growth factors found a benefit with the use of growth factors at this lower risk level. Previously, it had been thought that G-CSFs would be of greatest benefit in severe, protracted neutropenia because patients experiencing this toxicity develop comparably more severe infections. However, recent data show that individuals receiving milder chemotherapy and in whom the marrow is therefore not as suppressed may benefit more from growth factors because there are more marrow cells that can respond. Based on this finding, the indication for G-CSFs has been widened to include not only patients who are very likely to develop febrile neutropenia but also those less likely to develop this side effect.

**H&O** What other advances are reflected in the new guidelines?

**DD** Much progress has been made in terms of defining risk factors for fever and neutropenia following treatment with chemotherapy, and these new understandings have also been incorporated into the ASCO guidelines. Today, it is easier than it was a few years ago to define populations who are likely to fall into the 20% probability threshold and who should therefore receive G-CSF as a preventive measure against infection. In addition, we can now better identify patients at greatest risk of developing febrile neutropenia, which would be another population of special interest to clinicians.

**H&O** Does the lower threshold required for initiating G-CSF therapy alter the approach to monitoring patients receiving chemotherapy?

**DD** In some respects it does and in others it does not. A widely used strategy during the early development of CSFs was secondary prevention. With this approach, the WBC response was carefully monitored during the first cycle of chemotherapy. Patients who experienced decreasing WBC counts would be recommended for

treatment with a growth factor during the second cycle of chemotherapy. This strategy involved a greater degree of monitoring than is recommended in the 2006 ASCO guidelines. The current recommendation is that if the regimen is associated with severe myelosuppression or if a patient can be predicted, based on age, comorbidities, and other treatments, to be at risk for neutropenia, it is not necessary to conduct careful monitoring. Rather, the emphasis is on prediction.

**H&O** So with the new understandings about risk factors, the emphasis has shifted from monitoring to prediction?

**DD** That is correct. The healthcare professional can review a list of risk factors and determine in advance whether preventative CSF treatment might be necessary before chemotherapy is begun.

**H&O** Could you describe the newly added category for the use of CSFs in older patients?

**DD** The proportion of patients undergoing cancer treatment who are over the age 65 or 70 years is very significant and clinicians must consider how to integrate geriatric care with oncology care. Older patients have older hematopoietic systems and often have comorbidities. Thus, aging is associated with certain responses to chemotherapy as well as concomitant ailments such as diabetes, lung disease, and renal disease. These two components must be carefully considered when administering chemotherapy to older patients. In addition, the patterns of malignancy may be different in older patients compared with younger patients. For example, a disease may be more or less aggressive. This difference must also be factored into treatment approaches.

Traditionally, the response to these considerations has been to give older patients less treatment, based on a clinician's estimate about what a patient will be able to tolerate. However, as chemotherapy strategies have become more effective, specific approaches for delivering more treatment to older patients have been developed; administering G-CSFs is one way to accomplish this goal.

The 2006 ASCO guidelines broaden the indication for the use of G-CSFs in older patients, so that, going forward, older patients will likely receive more chemotherapy and also more CSFs.

**H&O** Is older age associated with a different response to CSFs?

**DD** No. Several years ago, a study of the response of older patients to CSFs showed that older age is not associated with an impaired response to CSFs. This finding is a very

important part of the basis for the broadened indication of CSFs in elderly patients.

**H&O** Does older age change the degree of monitoring that must be done during chemotherapy treatment?

**DD** No. Elderly patients are expected to respond similarly to younger patients. Of course, if a patient has comorbidities, it must be appreciated that the stress of chemotherapy may lead to developments with other conditions, and that specific illnesses carry specific requirements for care. However, with regard to chemotherapy and CSF use, the guidelines for monitoring are the same for all patients.

**H&O** What do the new guidelines recommend for the use of growth factors in individuals exposed to radiation?

**DD** In general, for patients receiving radiation therapy as part of their treatment or as a primary treatment, the traditional approach for avoiding neutropenia was to follow WBC counts and ease therapy when counts began to fall. However, it has been learned that CSFs can be given concomitantly with radiation therapy, allowing patients to complete their radiation treatment as originally scheduled. The new ASCO guidelines include a special comment pertaining to patients exposed to lethal total body irradiation, as could occur with radiation accidents. Such individuals should receive prompt administration of G-CSF or pegylated G-CSF to ameliorate or reduce the injury. Thus, the same principles apply to radiation accidents as apply to radiation therapy.

**H&O** What are the priorities for future research with CSFs?

**DD** One of the biggest changes in chemotherapy over the past few years has been the use of dose-dense therapy, in which treatment is given within a shorter time frame. This change has been possible only because of the availability of G-CSFs. The impact of this change on patient outcomes is only beginning to be understood, with the first data in breast cancer and lymphoma now becoming available. The integration of CSF support into this chemotherapeutic strategy will likely be a significant area of study as the benefits of dose-dense chemotherapy continue to be realized. Another area of focus pertains to the use of biologic agents in combination with chemotherapy. It is not yet clear how these newer agents will interact with CSFs.

Finally, combining antibiotics and growth factors is another interesting area of research. A study published in 2005 indicated that adding CSFs to prophylactic antibi-

otics conferred a significant degree of benefit. We need to learn more about the interplay of antibiotics and CSFs. In general, antibiotics are recommended for treatment and CSFs are recommended for prevention, but this categorization oversimplifies their use. In the coming years, we may see a refinement in the use of CSFs for the treatment of infection and, similarly, in the use of antibiotics for prevention in very selective circumstances.

### Suggested Reading

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