Anumber of novel and targeted agents for treating cancer have been introduced in recent years. Nevertheless, chemotherapy remains the mainstay of treatment in the majority of patients, and myelosuppression—especially neutropenia—represents the primary dose-limiting toxicity of chemotherapy. Therefore, chemotherapy-induced neutropenia remains a central concern in the safe and effective delivery of chemotherapy. The consequences of chemotherapy-induced neutropenia are far-reaching, from short- and long-term clinical effects to economic and quality-of-life issues.[1] The risk of infection correlates with both the depth and the duration of neutropenia. Febrile neutropenia is treated as a potentially life-threatening emergency, with immediate hospitalization and prompt administration of broad-spectrum antibiotics representing the standard of care.[2] In addition, patients with severe neutropenia and febrile neutropenia have lower quality of life and physical well-being.[3-5] Perhaps the most important potential effects of chemotherapy-induced neutropenia are subsequent reductions in chemotherapy dose intensity, due to dose reductions and treatment delays that are intended to lessen the incidence of neutropenia and its complications.[6] Clinical studies have demonstrated the importance of maintaining chemotherapy dose intensity in long-term survival in patients with responsive and potentially curable malignancies.[7-9] Prophylactic colony-stimulating factor (CSF) has been shown to reduce the severity and duration of severe neutropenia and the risk of febrile neutropenia, as well as enable the delivery of full chemotherapy dose intensity.[10-13] Guidelines established by the American Society of Clinical Oncology (ASCO) for use of the CSFs are based primarily on the expected risk of febrile neutropenia associated with specific chemotherapy regimens. Primary prophylaxis with CSF is recommended when the chemotherapy regimen is associated with a 40% likelihood of hospitalization for febrile neutropenia.[14] In fact, improved economic analyses suggest that a cost savings is likely with the use of prophylactic CSF when the risk of febrile neutropenia exceeds 20%. This approach requires assessing the myelosuppressive potential of the chemotherapy regimen; although some regimens are clearly more myelosuppressive than others, the true incidence of severe neutropenia associated with most regimens is underreported and ill-defined.[15] The articles in this supplement discuss an alternative approach to the effective and cost-effective use of CSF through the development and application of clinical predictive or risk models. In the first article, I discuss such predictive models, which attempt to identify patients at increased risk of neutropenic complications to enable the targeted use of CSF in those patients, and not in those at low risk and thus less likely to benefit. Risk models reported to date have been developed retrospectively, in small numbers of patients, and only a few of them have been validated in separate patient populations. Consequently, a large nationwide patient registry has been developed to gather prospective data for creating more accurate and valid risk models for routine clinical use.[16] The second and third articles in this supplement focus on specific clinical settings: early-stage breast cancer (Chau Dang, Monica Fornier, and Clifford Hudis) and non-Hodgkin's lymphoma (Andrew Zelenetz). Because of the strong relation between chemotherapy dose and outcome in these two cancers, together with the fact that myelosuppression is a frequent cause of dose alterations, risk models have been most frequently developed for these cancers. The final article, by Lodovico Balducci, discusses prophylaxis with CSF in elderly patients. Studies have repeatedly found that age is a risk factor for neutropenia and its complications[17] and that the risk is highest in the early cycles of chemotherapy.[18-20] Consequently, chemotherapy is often initiated at lower, substandard doses in the elderly in an effort to minimize myelosuppression and avert neutropenia—a practice that may be responsible for the poorer outcomes in older patients.[6,21] Elderly patients should therefore be considered a special population in whom early use of prophylactic CSF should be considered. In addition to age, other
patient-, disease-, and treatment-related measures are associated with an increased risk of neutropenia and its complications. Once validated, predictive models will be used for selecting such high-risk patients for CSF prophylaxis. Subsequent studies will be needed to evaluate the impact of targeted CSF prophylaxis using these models on the clinical, quality-of-life, and economic outcomes of cancer treatment.

Disclosures: The author(s) have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.


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