Primary Prophylaxis With Hematopoietic Colony Stimulating Factor: Insights From a Canadian Cost-Effectiveness Analysis

Scott A. Strassels, Michael Dickson, LeAnn B. Norris, Charles L. Bennett

Correspondence to: Scott A. Strassels, PharmD, PhD, 11003 Galleria Cove, Austin, TX 78759 (e-mail: scotts1@uw.edu).

In this issue of the Journal, Lathia et al. (1) modeled the cost-effectiveness of primary prophylaxis with filgrastim or pegfilgrastim against febrile neutropenia in patients with diffuse large B-cell lymphoma (DLBCL) undergoing chemotherapy from the perspective of a publicly funded health-care system. The inputs for the model were obtained from published literature and clinical practice. The model indicated that in the base case analysis, costs (in 2012 Canadian dollars) associated with no primary prophylaxis, or primary prophylaxis with 10 days of filgrastim, or a single dose of pegfilgrastim per cycle were $7314, $13,497, and $16,290, respectively. The incremental cost-effectiveness ratios for filgrastim vs no primary prophylaxis was $5.8 million per quality-adjusted life year (QALY) and for pegfilgrastim vs filgrastim primary prophylaxis was $2.6 million per QALY. In comparison with no prophylaxis, there was a slight increase in QALYs with filgrastim (0.2015 vs 0.2004) and pegfilgrastim (0.2024 vs 0.2004). However, this model was based on the important assumption (in accordance with current evidence) that the primary benefit of granulocyte colony-stimulating factor is in preventing chemotherapy-induced neutropenia and that there is no survival benefit associated with use of these drugs in persons with DLBCL (2–5). These results are in sharp contrast to a previously reported analysis in lymphoma patients where pegfilgrastim prophylaxis was associated with an incremental cost-effectiveness ratio of $6190 per QALY when a febrile neutropenia–related mortality benefit was assumed and $1677 per QALY when a long-term mortality benefit was assumed (6). On the other hand, a model of the cost-effectiveness of filgrastim, using a death state in the model and not including a mortality benefit found an incremental cost-effectiveness ratio of $700,000 per QALY. This estimate, similar to the estimates of Lathia et al. (1), is consistent with a conclusion that filgrastim is not cost-effective (7).

If primary prophylaxis with filgrastim or pegfilgrastim resulted in improvements in progression-free survival or overall survival, the strategy would become cost-effective. However, even though primary prophylaxis decreases by half the rate of febrile neutropenia in the first cycle of chemotherapy for DLBCL, the long-term beneficial effects appear to be unlikely. As demonstrated by sensitivity analysis, if costs of filgrastim were reduced to $70 per dose (60% reduction), the cost of the 10-day filgrastim strategy would be equal to the cost of the no primary prophylaxis strategy (secondary prophylaxis). Similarly, if the cost of pegfilgrastim were reduced to $908 (63% reduction), the cost of the pegfilgrastim strategy would be equal to the cost of the no primary prophylaxis (secondary prophylaxis) strategy. With the advent of a new granulocyte colony-stimulating factor, it is possible that competitive pricing will result and true cost equivalency could be achieved. In Europe, the use of biosimilar versions of filgrastim and pegfilgrastim in the past few years has made such a goal possible.

Although this model used the median age of persons diagnosed with lymphoma, the recommendations from this cost-effectiveness model are in line with those reported recently in a clinical review of filgrastim and pegfilgrastim as primary prophylaxis against febrile neutropenia for a 55-year-old patient receiving rituxan, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) (8). In contrast, a report by Potosky et al. found that 96% of filgrastim use in lung and colorectal cancer patients was not supported by evidence-based guidelines (9). With current annual filgrastim sales at $5.2 billion, decreasing use of filgrastim and pegfilgrastim where appropriate, as in the setting of primary prophylaxis for younger persons with DLBCL receiving a first cycle of R-CHOP, would reduce costs without adversely affecting clinical outcomes.

The findings from this model are similar to those reported by Weeks et al. when evaluating the cost-effectiveness of immune globulin for infection prevention among persons with chronic lymphocytic leukemia—estimated at $6 million per QALY (10). Sensitivity analyses in that study indicated that if subgroups of patients who would achieve a survival benefit with immune globulin could be identified, then this could be proven to be a cost-effective strategy for those patients. Similarly, in the setting of DLBCL, identification of high-risk patient subgroups could yield similarly favorable cost-effectiveness estimates.

The Lathia et al. (1) analysis is limited in that some data were used from studies conducted in populations other than the one considered in the analysis and the clinical data for febrile neutropenia rates for lymphoma patients receiving pegfilgrastim were based on patients who were experiencing a disease relapse and received chemotherapy other than R-CHOP (11). Despite these limitations, sensitivity analyses indicated that without a substantial price reduction or identification of survival benefits, primary prophylaxis with either filgrastim or pegfilgrastim is unlikely to be cost-effective from a health-system perspective. Until one or both of these events occur, primary prophylaxis with filgrastim or pegfilgrastim should be regarded as an expensive therapy that is not recommended for use as primary prophylaxis for persons with DLBCL who do not have comorbid illnesses or who are older.
Beyond the clinic, this analysis touches on the role of supportive and symptomatic care in persons who have cancer and the use of cost-effectiveness criteria in determining coverage of supportive care agents. Given the median age of diagnosis noted by Lathia et al. (1), about 50% of persons with lymphoma will qualify for Medicare at diagnosis; thus how insurers make use of cost-effectiveness information has important implications for national health policy (12). Furthermore, incremental costs per QALY (or other measure of time) are challenging to estimate and use in clinical practice and policy making, particularly estimates of survival benefits and longer term benefits as well as inclusion of nonclinical outcomes such as hospital avoidance. Additionally, situations like the one modeled here, in which the time horizon is very short, complicate the use of outcomes like the QALY. Despite this understanding, the optimal choice of an outcome to model in persons with cancer remains incompletely understood (13). Last, the importance of patient-reported outcomes is rising. In the current case, the potential to avoid hospitalizations is likely to be important from the patient’s perspective. Although this trend does not change the conclusions Lathia et al. make regarding prophylactic use of filgrastim and pegfilgrastim, patient satisfaction, ability to function, and time preferences are likely to play an increasing role in future coverage and clinical use decisions.

References


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Affiliations of authors: Austin, TX (SAS); Department of Clinical Pharmacy and Outcomes Sciences, South Carolina College of Pharmacy, Columbia, SC (MD, LBN, CLB); Department of Pharmacy Services, William Jennings Bryan Dorn VA Medical Center, Columbia, SC (LBN); Hollings Cancer Center of the Medical University of South Carolina, Charleston, SC (CLB); Arnold School of Public Health, University of South Carolina, Columbia, SC (CLB).

Cancer Incidence Among Specific Asian and Pacific Islander Populations in the Unites States

Dee W. West, Paul K. Mills

Correspondence to: Dee W. West, PhD, Public Health Institute, Cancer Registry of Greater California, Sacramento, CA 95825 (e-mail: dwest@crgc-cancer.org).

To identify disease etiology and its consequences, epidemiologists compare disease rates in different populations, geographic areas, and time periods. These statistical comparisons become difficult when diseases are relatively rare (eg, most cancers), and this problem is often resolved by broadening the definition of the groups (eg, all Asians or Pacific Islanders), geographic areas (eg, many

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