Economic Analysis of Prophylactic Pegfilgrastim in Adult Cancer Patients Receiving Chemotherapy

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ABSTRACT

Objectives: Neutropenia and its complications, including febrile neutropenia (FN), are a common side effect of cancer chemotherapy. Results of clinical trials showed that prophylactic use of granulocyte colony-stimulating factors (G-CSF) is effective in preventing FN. In this study, the cost effectiveness (measured as cost per quality-adjusted time [days]) of three treatment alternatives were evaluated: no G-CSF, filgrastim administered daily for 7–12 days after chemotherapy, and a pegylated form of G-CSF pegfilgrastim, administered once per cycle.

Methods: A cost-utility model based on standard clinical practice of treating FN with immediate hospitalization or with ambulatory treatment, from a societal perspective was developed. Direct medical cost estimates for hospitalization were derived from claims data reported by 115 US academic medical centers. Indirect medical costs, productivity costs, probabilities, and utilities are based on published literature. Results were subjected to sensitivity analyses and 95% confidence intervals are based on a Monte Carlo simulation.

Results: Mean estimated costs/day of hospitalization were $1984 (SD $1040, N = 24,687) for surviving patients and $3139 (SD $2014, N = 1437) for dying patients. Under baseline conditions, pegfilgrastim dominated both filgrastim and no G-CSF, with expected costs and effectiveness of $4203 and 12.361 QALDs for no G-CSF, $3058 and 12.967 QALDs for pegfilgrastim, and $5264 and 12.698 QALDs for filgrastim.

Conclusions: This cost-utility analysis provides strong evidence that pegfilgrastim is not only cost-effective but also cost-saving in most common clinical and economic settings. There appear to be both clinical and economic benefits from prophylactic administration of pegfilgrastim.

Keywords: cancer, cost analysis, decision models, febrile neutropenia, granulocyte colony-stimulating factors, neutropenia.

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Introduction

Neutropenia is a common chemotherapy-related complication. Neutropenia is defined as a below normal count of neutrophils (white blood cells), which are particularly important in fighting and preventing infection. Febrile neutropenia (FN), defined as the presence of both neutropenia and fever, routinely prompts immediate hospitalization for evaluation and administration of empirical broad-spectrum antibiotics [1] and may subsequently result in chemotherapy dose delays or reductions [2]. It is estimated that in the United States, more than 60,000 neutropenia-related hospitalizations occur each year [3]. The costs associated with those hospitalizations add significantly to the direct medical costs of cancer treatment and pose a great financial burden in the overall care of cancer patients [4].

Considerable attention has been given in recent years to identifying FN patients at low risk of complications who may be candidates for outpatient treatment with antibiotics [5]. Although replacing hospitalization and intravenous (IV) antibiotic treatment with outpatient oral antibiotics holds promise for savings, a formal cost analysis of outpatient treatment demonstrated only limited economic effect on the overall cost of cancer treatment as low-risk patients account for a small proportion of the overall costs of cancer patient care for FN [6].

Randomized controlled trials (RCTs) have demonstrated that prophylactic granulocyte colony-stimulating factors (G-CSF; filgrastim) initiated after myelosuppressive chemotherapy and administered daily until neutrophil recovery is effective in reducing the incidence of FN by as much as 50% [7,8]. Patients treated with a G-CSF have shorter lengths of hospitalization (LOS) and shorter time to neutrophil recovery than control subjects [9]. Recently updated guidelines of the American Society of Clinical Oncology (ASCO) and the European Organization for Research and
Treatment of Cancer (EORTC) recommend primary (first cycle) prophylactic G-CSF administration for chemotherapy regimens associated with an FN incidence rate of 20% or greater, or when special circumstances exist, such as history of recurrent FN or more advanced cancer [10–12].

A new, long-acting pegylated form of G-CSF, pegfilgrastim (Neulasta; Amgen Inc., Thousand Oaks, CA) administered once per chemotherapy cycle, has been shown in recent RCTs to be at least as effective and safe as filgrastim [13,14], demonstrating a relative risk reduction (RRR) for FN greater than 90% [15]. Because of its convenient administration to both the patient and medical staff and potentially increased effectiveness, pegfilgrastim often displaces filgrastim in the United States whenever it is being reimbursed by payers [16]. Many patients receiving conventional systemic chemotherapy are not receiving primary prophylaxis with G-CSF [2,17], suggesting that many physicians still consider “watchful waiting” a valid treatment option during the first cycle of chemotherapy.

Although the economic impact of filgrastim has been well studied, indicating that primary prophylaxis in patients receiving chemotherapy can be cost-effective compared with “no G-CSF” (attributed mainly to a decreased risk of FN) [18,19], and despite considerable clinical interest and wide-scale use of pegfilgrastim, a thorough economic evaluation of pegfilgrastim has not been previously reported. The objective of this analysis is to evaluate the economic impact of pegfilgrastim compared with filgrastim and no G-CSF when administered prophylactically during the first cycle of chemotherapy.

**Methods**

**Decision Analysis**

A cost-utility (CU) model was created to compare the economic impact of three treatment alternatives: primary prophylactic use of pegfilgrastim, primary prophylactic use of filgrastim, and no prophylactic G-CSF (Fig. 1). This model was premised on common clinical practice, in which patients receiving chemotherapy are at risk for developing FN. Patients experiencing FN are then managed either as inpatients or as outpatients based on their risk of serious complications or death. An outpatient treatment includes the administration of IV antibiotics and may be followed by hospitalization if the patient’s condition deteriorates.

The modeled population consists of patients between the ages of 18 and 65 years old, hospitalized between 1995 and 2003 for a solid tumor cancer as identified by the International Classification of Disease, Ninth version, Clinical Modification (ICD-9-CM) codes 140.00 to 199.00, and also with a diagnosis of neutropenia (agranulocytosis), ICD-9-CM code 288.00. Costs and LOS were estimated for surviving and dying patients separately.

The analysis was performed from the societal perspective, incorporating direct as well as indirect medical costs, productivity costs, and travel costs (Table 1). Costs are measured in US dollars, adjusted to 2005 using the Consumer Price Index—Urban for medical care [29]. Effectiveness is measured in quality-adjusted life-days (QALDs). The time horizon is the first cycle of chemotherapy defined as 21 days, when most patients receive full-dose chemotherapy, often
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