Therapeutic Use of Filgrastim for Established Febrile Neutropenia Is Cost Effective Among Patients With Solid Tumors and Lymphomas

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ABSTRACT

Purpose: With the emergence of biosimilar filgrastim to the market, there is a gradual decrease in the listed price of the originator product of filgrastim over the years, and this could have an impact on the cost-effectiveness of filgrastim in the treatment of febrile neutropenia (FN). A cost-effectiveness analysis would allow clinicians to make informed decision when considering the therapeutic filgrastim among low-risk FN patients. This study aims to evaluate the cost-effectiveness of adding therapeutic filgrastim to antibiotics in the treatment of established FN among patients with solid tumors and lymphomas.

Methods: A decision tree model was created to compare two treatment options for established FN as follows: (1) antibiotics alone (standard care) and (2) antibiotics with therapeutic filgrastim (comparator). The target population was a hypothetical cohort of adult cancer patients with solid tumors or lymphomas hospitalized with FN in Singapore. The analysis was performed from a hospital's perspective over a 21-day time horizon. The main outcome measures included costs, quality-adjusted life year (QALY) and incremental cost-effectiveness ratio (ICER). One-way sensitivity analysis and probabilistic sensitivity analysis were conducted to evaluate the robustness of the results.

Findings: Compared with antibiotics alone, the treatment strategy of antibiotics with therapeutic filgrastim was a dominant choice, incurring a cost saving of US$125 per patient (comparator versus standard care: US$9110 versus US$9235) and additional health benefit of 0.0007 QALY gained per patient (comparator versus standard care: 0.0450 versus 0.0443). Model results were robust against the parameter variations in the one-way sensitivity analyses, but increasing the cost of filgrastim beyond US$87 per injection would increase the ICER to >US $50,000/QALY. Furthermore, the strategy of antibiotics with therapeutic filgrastim was the preferred choice (dominant or cost-effective) in 83.7% of the model iterations at a willingness-to-pay threshold of US$50,000/QALY.

Implications: From a hospital's perspective, the therapeutic filgrastim, in conjunction with antibiotics, in the treatment of FN is cost effective. This provides evidence to support the routine use of filgrastim for the treatment of FN among adult cancer patients with solid tumors and lymphomas. (*Clin Ther.* 2017;39:1161–1170)

Key words: cost-effectiveness analysis, febrile neutropenia, filgrastim, treatment.

INTRODUCTION

Febrile neutropenia (FN) is a serious oncologic emergency experienced by cancer patients receiving myelosuppressive chemotherapy. One recent study in Singapore identified that FN had an incidence of around 19.5% among patients with solid tumors or lymphomas and that FN was the most common reason for unwanted hospitalizations.[1] FN is associated with a significant economic burden on patients. In Singapore, we have reported that the cost of inpatient FN management was around US $4193 per episode, and FN patients who had

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developed severe sepsis were associated with a significantly higher economic burden.[2]

Filgrastim is a granulocyte colony-stimulating factor (G-CSF) that stimulates neutrophil production. The prophylactic use of G-CSF, including filgrastim, has been supported by the current guideline to prevent FN.[3] However, the therapeutic use of G-CSF for established FN is not recommended among low-risk FN patients, such as patients with solid tumors or lymphomas.[3–5] One recent meta-analysis of randomized controlled trials suggested that patients receiving G-CSF plus antibiotics had shorter duration of FN and antibiotics use than patients receiving antibiotics alone.[6] Therefore, the therapeutic use of filgrastim is expected to reduce patient's hospital length of stay (LOS) and to provide benefits on cost savings associated with reduced hospitalization and antibiotics use.

With the emergence of biosimilar filgrastim to the market, a gradual decrease in the listed price of the originator product of filgrastim has occurred over the years, and this could have an impact on the cost-effectiveness of filgrastim in the treatment of FN.[7] To our knowledge, cost-effectiveness studies that focus on the therapeutic use of filgrastim for established FN among patients with solid tumors and lymphomas are lacking. A cost-effectiveness analysis would allow clinicians to make informed decision when considering the therapeutic filgrastim among low-risk FN patients. Therefore, we designed this study with the primary objective to evaluate the cost-effectiveness of therapeutic filgrastim in the treatment of FN among adult patients with solid tumors and lymphomas.

PATIENTS AND METHODS

A decision tree model was constructed by using TreeAge Pro 2013 (TreeAge Software, Inc, Williamstown, Massachusetts) to compare two treatment options for FN as follows: (1) antibiotics alone (standard care) and (2) antibiotics with therapeutic filgrastim (comparator). The antibiotic treatment for FN in both standard care and comparator arms followed the approaches recommended by the Infectious Disease Society of America guideline.[8] Empiric antibiotic therapy included an antipseudomonal β-lactam agent, such as cefepime, carbapenem (meropenem or imipenem-cilastatin), or piperacillin-tazobactam.[8] Other antibiotics, such as aminoglycosides, fluoroquinolones, and/or vancomycin, may be considered in patients with complicated presentations (eg, hypotension and pneumonia) or suspected/proven antimicrobial resistance.[8] In the comparator group, the therapeutic filgrastim was administered daily until patients' absolute neutrophil count (ANC) recovered (ANC $\geq 2.0 \times 10^9$/L). In this model, the time horizon was set as 21 days to represent the interval between each chemotherapy cycle. No discounting was applied because of the short time horizon in this model. The perspective was taken from a Singaporean hospital, and only direct medical cost was considered in this study.

Definitions

FN was defined as a single episode of fever $\geq 38.3^\circ$C or fever $\geq 38.0^\circ$C for at least 1 hour and an ANC of $< 0.5 \times 10^9$/L.[8] Grade IV neutropenia was set as having an ANC of $< 0.5 \times 10^9$/L.[9] The duration of grade IV neutropenia was the number of days with ANC $< 0.5 \times 10^9$/L. Time to ANC recovery was the duration from FN onset date until patients' ANC increased to 2.0×10^9/L. In this study, serious complication was defined as the occurrence of severe sepsis during the hospitalization. LOS was the overall duration from FN onset date until patient was discharged from the hospital.

Model Structure

The model structure is shown in Figure 1. The design of this model is based on the Infectious Disease Society of America guideline[8] and clinicians' discussion to reflect the local treatment pattern for established FN, and the face validity of this model was endorsed by the clinicians who manage FN. Several studies have reported the effectiveness of filgrastim on reducing the duration of grade IV neutropenia.[6,10] Therefore, the duration of grade IV neutropenia was included in this model. The duration of grade IV neutropenia was categorized into the following two groups: (1) grade IV neutropenia ≤ 3 days and (2) grade IV neutropenia > 3 days, which was based on a previous study in Singapore, showing that the mean duration of grade IV neutropenia was around 2 to 3 days.[11] Serious complication was considered because prolonged duration of grade IV neutropenia would increase the risk of a patient developing serious complications.[12]