Executive Summary

Introduction

Granulocyte colony stimulating factor (G-CSF) stimulates the proliferation of neutrophils in bone marrow. In clinical practice, it can be used in febrile neutropenic patients to reduce the duration of febrile neutropenia and infectious events. In recent years, guidelines developed in Europe or U.S. recommended that prophylactic G-CSF should be used in patients who received the cheomotherapeutic regimen that show the risk of febrile neutropenia over 20%. However, in Korea prophylactic use of G-CSF is prohibited due to reimbursement problem.

Methods

Multidisciplinary committee was formed with representatives from each academic society in oncology, hematology, and methodology. Using systematic methods, major guidelines for utilizing G-CSF were searched and selected. Selected guidelines were appraised by committee members with Appraisal of Guidelines for Research and Evaluation instrument (AGREE) tool.

The committee also collected clinical data of patients who were treated with cancer chemotherapy in university affiliated hospitals. Included type of cancer was breast cancer, lymphoma, head and neck cancer, and sarcoma. Data of baseline characteristics, the information related to febrile neutropenia, and that related to G-CSF use were collected. Because each hospital used different prophylactic strategy (prophylactic use versus rescue therapy), cost-effectiveness analysis was done with neoadjuvant DA (docetaxel, adriamycin) regimen used in breast cancer.

Results

All of the major guidelines of Europe or U.S. recommend prophylactic use of G-CSF in patients who receive the cheomotherapeutic regimen that show the risk of febrile neutropenia over 20%. If the risk of febrile neutropenia is between 10 and 20%, prophylaxis may be considered according to patients-related risk factors such as age, previous episodes of febrile neutropenia, performance status, and so on. Accepting these major recommendations, the committee decided to adapt EORTC (European Organisation for Research and Treatment of Cancer) guideline because it won the highest scores in “rigour of development” domain.

In retrospective chart review, frequency of febrile neutropenia after each chemotherapeutic regimens was examined: AC regimen (adriamycin+cyclophosphamide) in breast cancer showed 11.1%, DA regimen (docetaxel+adriamycin) in breast cancer, 20.1%, CHOP regimen (cyclophosphamide+adriamycin+vincristin+prednisolone) in lymphoma 34.8%, R-CHOP (rituximab+CHOP), 22.1%, DFP (docetaxel+5-FU+cisplatin) in head and neck cancer, 18.4%, respectively. Prophylactic strategy showed smaller cost and fewer febrile neutropenia events than rescue strategy in neoadjuvant DA regimen.

Recommendations that the committee suggests were as follow:

1. Patient-related risk factors should be evaluated in the overall assessment of febrile neutropenia risk prior to administering each cycle of chemotherapy. Patient-related risk factors of febrile neutropenia are elderly patients (aged 65 and over), advanced stage of disease, experience of previous episode(s) of febrile neutropenia, lack of G-CSF use and lack of antibiotic prophylaxis.

2. Consideration should be given to the elevated risk of febrile

neutropenia when using certain chemotherapy regimens that known to elevate the risk of febrile neutropenia.

3. In situations where dose-dense or dose-intense chemotherapy strategies have survival benefits, prophylactic G-CSF should be used as a supportive treatment.

4. When assessing febrile neutropenia risk, the clinician should take into account patient-related risk factors (recommendation 1), the chemotherapy regimen and associated complications (recommendations 2 and 3) and treatment intent (recommendation 3). If the patient is at ≥20% overall risk of febrile neutropenia, prophylactic G-CSF is recommended. When using chemotherapy regimens associated with a febrile neutropenia risk of 10–20%, particular attention should be given to the assessment of patient characteristics that may increase the overall risk of febrile neutropenia.

5. Treatment with G-CSF for patients with solid tumors and ongoing febrile neutropenia is indicated only in special situations. These are limited to those patients who are not responding to appropriate antibiotic management and who are developing life-threatening infections.

6. Filgrastim, lenograstim and pegfilgrastim have clinical efficacy and we recommend the use of any of these agents to prevent febrile neutropenia and febrile neutropenia related complications, where indicated.