Complete Summary

GUIDELINE TITLE

Guidelines on the use of colony-stimulating factors in haematological malignancies.

BIBLIOGRAPHIC SOURCE(S)

Pagliuca A, Carrington PA, Pettengell R, Rule S, Keidan J, Haemato-Oncology Task Force of the British Committee for Standards in Haematology. Guidelines on the use of colony-stimulating factors in haematological malignancies. Br J Haematol 2003 Oct;123(1):22-33. [96 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- January 24, 2008, Leukine (sargramostim): Voluntary market suspension of the current liquid formulation of sargramostim, a granulocyte-macrophage colony-stimulating factor (GM-CSF), because of an upward trend in spontaneous reports of adverse reactions, including syncope (fainting). The lyophilized form of the drug is not affected. See the U.S. Food and Drug Administration (FDA) web site for more information.

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SCOPE

DISEASE/CONDITION(S)

Haematological malignancies, including:

- Acute myeloid leukaemia (AML)
- Acute lymphoblastic leukaemia (ALL)
- Myelodysplastic syndromes (MDS)
- Aplastic anaemia (AA)
- Bone marrow failure syndromes
- Non-Hodgkin's lymphoma (NHL)
- Hodgkin's disease (HD)
- Lymphoblastic lymphoma (LL)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness

CLINICAL SPECIALTY

Hematology
Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present recommendations for primary versus secondary prophylaxis with colony-stimulating factors (CSFs), and specific evidence and recommendations for the use of CSFs in the various haematological malignancies and transplant procedures, including those from the most recent update of the American Society of Clinical Oncology (ASCO) guidelines (summarized in Appendix 1 of the original guideline document)

TARGET POPULATION

Patients with hematologic malignancies

INTERVENTIONS AND PRACTICES CONSIDERED

Colony-stimulating factors (CSFs):

1. Primary prophylaxis
2. Secondary prophylaxis
3. Adjunctive treatment
4. In association with chemotherapy
5. For peripheral blood progenitor cell (PBPC) mobilization

6. After peripheral blood progenitor cell (PBPC) and bone marrow transplantation (BMT)

MAJOR OUTCOMES CONSIDERED

- Response to therapy
- Incidence of infection
- Adverse events
- Quality of life
- Survival

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A systematic review of the literature was undertaken from 1986 up to March 2002. The following diseases and transplant procedures were assessed:

- Acute myeloid leukaemia (AML)
- Acute lymphoblastic leukaemia (ALL)
- Myelodysplastic syndromes (MDS)
- Aplastic anaemia (AA)
- Non-Hodgkin's lymphoma
- Hodgkin's disease
- Lymphoblastic lymphoma
- Peripheral blood progenitor cell (PBPC) mobilization and transplantation

Studies were identified by searching the following databases:

- Medline
- EMbase
- Cancerlit
- Cochrane (UK) – Database of systematic reviews
    - The Cochrane Controlled Trials Register
    - Database of Abstract of Review of Effectiveness

Medline, EMbase and Cancerlit were searched to identify any randomized controlled trials (RCTs) using a modified version of the Cochrane Collaboration search strategy. The Task Force used only part of the complex Cochrane strategy using the OVID search strategy of RCT, controlled clinical trial, RCTs, random allocation, double-blind method, single-blind method, clinical trial, comparative study as search lines. Authors of trials were not contacted for further information. More general search strategies were used to identify non-randomized comparator studies and, where required, case histories. Meeting abstracts were hand

searched to ensure no information was missed. The Task Force used previous papers to identify references that were not otherwise found.

NUMBER OF SOURCE DOCUMENTS

Search strategies identified over 1500 citations. From the titles and abstracts of these papers, the systematic review process identified 299 publications as potentially relevant (98 lymphoma, 117 leukaemia, 36 peripheral blood progenitor cell [PBPC] transplantation, 24 PBPC mobilization and 24 post-PBPC and bone marrow transplant [BMT]).

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The definitions of the types of evidence and the grading of recommendations used in this guideline originate from the US Agency for Health Care Policy and Research and are set out in the following:

Statements of Evidence

Ia Evidence obtained from meta-analysis of randomized controlled trials.

Ib Evidence obtained from at least one randomized controlled trial.

IIa Evidence obtained from at least one well-designed controlled study without randomization.

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Studies were classified as follows:

- Prospective randomized controlled trial (RCT)

- Prospective cohort studies with a non-randomized comparator (including historical controls)
- Retrospective cohort studies with non-randomized comparator
- Case histories

For each disease or transplant procedure, a decision was made as to which level of evidence should be considered based on the number of trials and patients. If sufficient evidence was available from RCTs, then no other evidence was reviewed. Otherwise, all the other categories were included in the search.

Full papers relating to the highest levels of evidence in each disease or transplant procedure were ordered and reviewed by at least one clinical reviewer. When studies generated multiple publications the most recent publications containing sufficient information were used. Quantitative analysis of the publications was not performed.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The evidence for each of the guideline categories was assessed by the authors who represent specialists in the broad field of haematology and haemato-oncology and transplantation, within teaching hospitals and district hospitals. Draft guidelines were written based on the level of evidence supporting each statement.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations

A. Requires at least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)
B. Requires the availability of well-conducted clinical studies but no randomized clinical trials on the topic of recommendation. (Evidence levels IIa, IIb, III)
C. Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

COST ANALYSIS

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The draft guidelines were reviewed by the haemato-oncology task force of the British Committee for Standards in Haematology, and then distributed for peer review to 60 UK haematologists. The final version was then ratified by the haemato-oncology task force and the British Society for Haematology Committee.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence **(I–IV)** and strength of recommendations **(A–C)** are defined at the end of the "Major Recommendations" field.

Prophylactic and Adjunctive Use of Colony-Stimulating Factors (CSFs)

- Primary prophylaxis is not routinely recommended unless the expected incidence of febrile neutropenia is greater than 40% (**level IIa, grade B**).
- Secondary prophylaxis cannot be routinely justified because of a lack of available evidence but is indicated for tumours in which dose reduction/dose delay would compromise overall survival (**level III, grade B**).
- Adjunctive treatment is not recommended for patients with uncomplicated febrile neutropenia (**level Ib, grade A**) but should be considered in patients with the poor prognostic factors listed in the text (**level IV, grade C**).

Use of CSFs in Association With Chemotherapy

- Acute myeloid leukaemia (AML). The routine use of CSF is recommended after consolidation chemotherapy (**level Ib, Grade A**). CSF is recommended after induction if it is appropriate to reduce hospital stay or antibiotic usage.
- Acute lymphoblastic leukaemia (ALL). Granulocyte colony-stimulating factor (G-CSF) is indicated to reduce the severity of neutropenia following intensive phases of therapy (**level Ib, grade A**).
- Myelodysplastic syndromes (MDS). CSFs are indicted to reduce the severity of neutropenia in patients receiving intensive chemotherapy **(level Ib, grade A**). CSFs are also recommended on an intermittent basis for patients with neutropenia and infection (**level IV, grade C**), but continuous prophylactic use is not routinely justified.
- Aplastic anaemia. There is insufficient evidence to make any general recommendations and hence patients should be given CSFs only on an individual therapeutic trial basis (**level IV, grade C**).
- Bone marrow failure syndromes. G-CSF is recommended when improvement of neutrophil count is appropriate (**level III, grade B**).
- Malignant lymphomas. There is evidence to support the routine use of CSFs to reduce the incidence of infection, chemotherapy delay and hospitalization especially when the risk of febrile neutropenia exceeds 40% (**level Ia, grade A**). There is also emerging evidence of improved survival with G-CSF-supported dose intensification in elderly patients with high-grade non-Hodgkin's lymphoma (NHL) (**level Ib, grade A**). At present, this evidence is insufficient to justify a change in policy in all patients with lymphoma, but elderly patients may benefit from G-CSF support.

CSFs for Peripheral Blood Progenitor cell (PBPC) Mobilization

- CSFs are indicated for the mobilization of PBPCs.

CSFs After PBPC and Marrow Transplantation

- CSFs are indicated to accelerate reconstitution after allogeneic and autologous PBPC transplantation or bone marrow transplantation (BMT) (**level Ib, grade A**).

Definitions:

Statements of Evidence

Ia Evidence obtained from meta-analysis of randomized controlled trials.

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Grades of Recommendations

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B. Requires the availability of well-conducted clinical studies but no randomized clinical trials on the topic of recommendation. (Evidence levels IIa, IIb, III)
C. Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of Colony-Stimulating Factors (CSFs) in patients with haematological malignancies, for prevention of neutropenia-associated infection, avoidance of chemotherapy dose reduction and dose delay, priming of certain types of malignant cells so that they are more sensitive to some cytotoxic agents, acceleration of reconstitution of bone marrow after allogeneic and autologous peripheral blood progenitor cell (PBPC) transplantation or bone marrow transplant (BMT).
- Use of CSFs may reduce the need for hospitalization and antibiotic therapy

POTENTIAL HARMS

Side effects of treatment

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- There is no evidence of any difference between the available Colony-Stimulating Factors (CSFs) (granulocyte colony-stimulating factor and granulocyte–macrophage colony-stimulating factor) in terms of efficacy or outcome providing the growth factors are given at the recommended dose. These guidelines therefore do not differentiate between the two types of agent, although specific agents may be referred to in the context of clinical trial results.
- While the advice and information in these guidelines is believed to be true and accurate at the time of going to press, neither the authors nor the publishers can accept any legal responsibility or liability for any errors or omissions that may have been made.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Oct

GUIDELINE DEVELOPER(S)

British Committee for Standards in Haematology - Professional Association

SOURCE(S) OF FUNDING

British Committee for Standards in Haematology

GUIDELINE COMMITTEE

Haemato-Oncology Task Force

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: Antonio Pagliuca, Kings College Hospital, London; Patrick A. Carrington, Trafford General Hospital, Manchester; Ruth Pettengell, St George's Hospital, London; Simon Rule, Derriford Hospital, Plymouth; Jane Keidan, King's Lynn and Wisbech Hospital, King's Lynn, UK

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the British Committee for Standards in Haematology Web site.

Print copies: Available from the BCSH Secretary, British Society for Haematology, 2 Carlton House Terrace, London SW1Y 5AF, UK; E-mail: janice@bshhya.demon.co.uk

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on September 27, 2006. The information was verified by the guideline developer on October 25, 2006. This summary was updated by ECRI Institute on February 26, 2008 following the U.S. Food and Drug Administration advisory/voluntary market withdrawal of the liquid formulation of Leukine (sargramostim).

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