



EBM Presentation

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Brief History (1)

- α This 4 year-old boy has a history of acute lymphoblastic leukemia under chemotherapy course of TPOG-ALL-2002 SR .
- α The chemotherapy course of TPOG-ALL-2002 SR was performed since 08.10.2006 . The general condition was stable during the previous chemotherapy course .



Brief History (2)

- ❑ Neutropenia (ANC : 165) was noted under the **reinduction chemotherapy** when he went to our OPD follow up on 10.25.2006 . But he denied any other discomfort or fever .
- ❑ Then fever has developed after 3 days (10.28 .2006) . At that time **ANC revealed 35 . High fever (38.5 degree)** with sorethroat , rhinorrhea was complained . Under the impression of **neutropenic fever** , he was admitted to our ward for further evaluation and management .
- ❑ Due to the neutropenic fever episode , his **next time chemotherapy delayed about 2 weeks** .



Background (1)

- Intensive cytotoxic chemotherapy -> profound neutropenia -> hospitalization for treatment of fever or cause potentially fatal infection
- In an attempt to decrease infectious complications, **colony-stimulating factors** have been used to reduce the duration and degree of neutropenia. Alternatively, **prophylactic antibiotics** have been administered to prevent the development of bacterial infections as a complication of the neutropenia.



Background (2)

■ Colony stimulating factors

-- prophylactic use following :

1. the administration of chemotherapy when neutropenia is anticipated ("primary prophylaxis")
2. during retreatment after a previous cycle of chemotherapy that caused febrile neutropenia ("secondary prophylaxis")
3. shorten the duration of severe chemotherapy-induced neutropenia without fever ("afebrile neutropenia").



PICO

Patient ~

acute lymphoblastic leukemia children under chemotherapy

Intervention ~

prophylactic administration of colony stimulating factors

Comparison ~

No treatment or placebo

Outcome ~

number of febrile neutropenia
time of neutropil counts recovery
incidence and length of hospitalization
incidence and length of treatment delays



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GUIDELINES ON THE USE OF COLONY-STIMULATING FACTORS IN HAEMATOLOGICAL MALIGNANCIES

British Journal of Haematology, 2003, 123, 22–33

 The following guidelines present recommendations for primary versus secondary prophylaxis with 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 .



METHODS

- α 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 (NHL) , Hodgkin's disease (HD) , Lymphoblastic lymphoma (LL) , PBPC mobilization and transplantation.
- α Studies were identified by searching the following databases:
 - Medline
 - EMbase
 - Cancerlit
 - Cochrane (UK)
 - Database of systematic reviews (CDSR)
 - The Cochrane Controlled Trials Register (CCTR)
 - Database of Abstract of Review of Effectiveness (DARE).Medline, EMbase and Cancerlit were searched to identify any randomized controlled trials (RCTs) using a modified version of the Cochrane Collaboration search strategy



PROPHYLACTIC AND ADJUNCTIVE USE

Recommendations

- **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**).

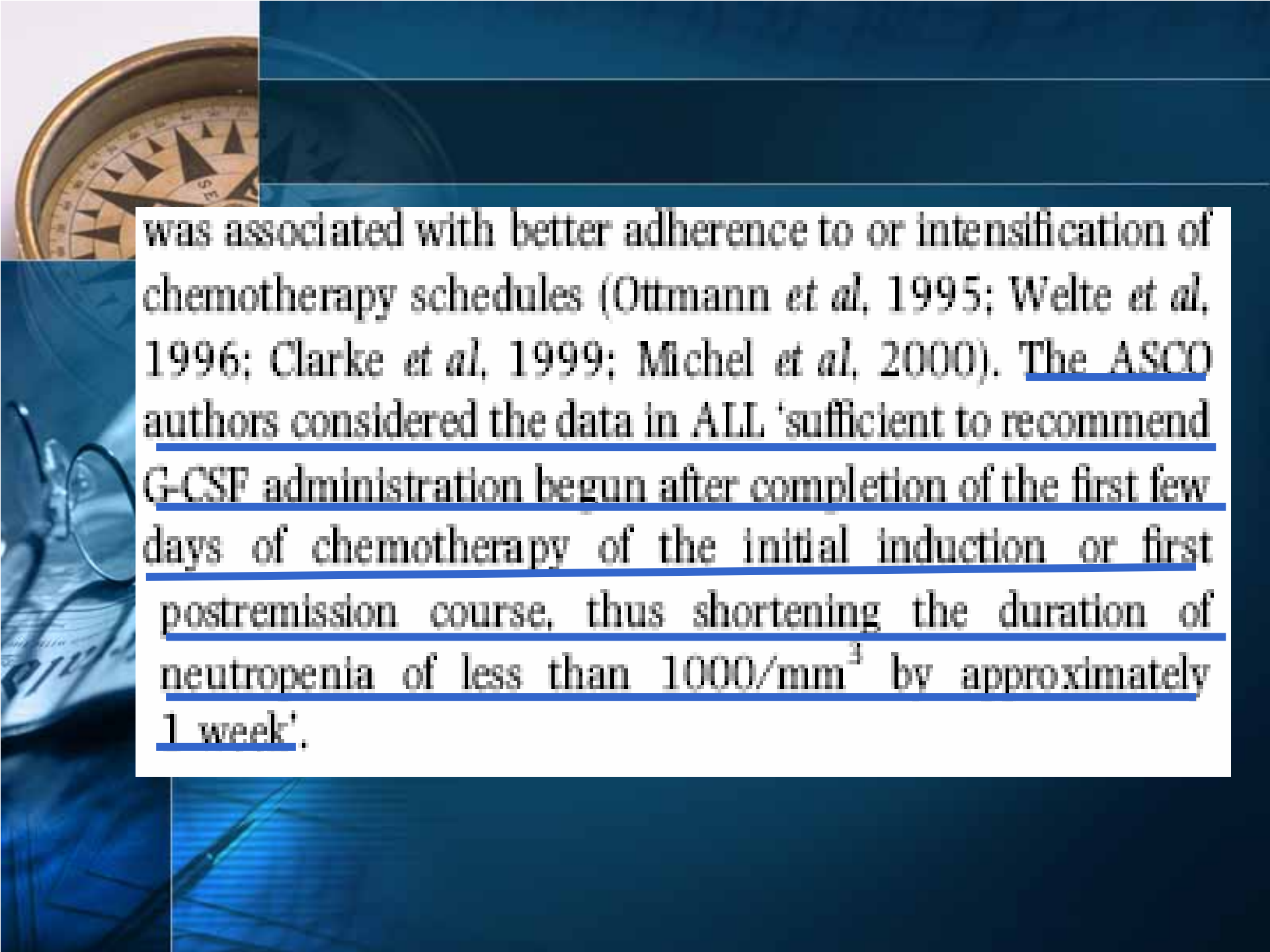


Recommendations

- ALL. G-CSF is indicated to **reduce the severity of neutropenia following intensive phases of therapy** (level Ib, grade A).
- The ASCO authors considered the data in ALL ‘sufficient to recommend G-CSF administration begun after **completion of the first few days of chemotherapy of the initial induction or first postremission course**, thus shortening the duration of neutropenia of less than $1000/\text{mm}^3$ by approximately 1 week’.

Acute lymphoblastic leukaemia

In six prospective, randomized trials in adults and children with ALL, CSFs (G-CSF in all cases) given during (Ottmann *et al*, 1995; Geissler *et al*, 1997; Larson *et al*, 1998), after (Pui *et al*, 1997) or between courses (Welte *et al*, 1996; Clarke *et al*, 1999) of chemotherapy has been shown to shorten the duration of neutropenia by up to 8 d when given to patients receiving induction and post-remission chemotherapy. As in AML, the effects on clinical parameters varied between the studies. The largest adult study showed a higher complete response rate in the G-CSF-treated group ($P = 0.04$) (Larson *et al*, 1998), but no trial showed any difference in terms of disease-free or overall survival. In five studies, there was evidence of a benefit with G-CSF in terms of fewer documented infections, shorter in-hospital stays and/or reduced antibiotic usage (Welte *et al*, 1996; Geissler *et al*, 1997; Pui *et al*, 1997; Larson *et al*, 1998; Clarke *et al*, 1999). Four studies also reported that treatment with G-CSF



was associated with better adherence to or intensification of chemotherapy schedules (Ottmann *et al*, 1995; Welte *et al*, 1996; Clarke *et al*, 1999; Michel *et al*, 2000). The ASCO authors considered the data in ALL 'sufficient to recommend G-CSF administration begun after completion of the first few days of chemotherapy of the initial induction or first postremission course, thus shortening the duration of neutropenia of less than 1000/mm³ by approximately 1 week'.



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Example: *(colchicine AND AND (fibrosis OR cirrhosis))*

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Example: *"colchicine therapy"*



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Colony stimulating factors for prevention of myelosuppressive therapy induced febrile neutropenia in children with acute lymphoblastic leukaemia

EC Sasse, AD Sasse, SR Brandalise, OAC Clark, S Richards

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EC Sasse, AD Sasse, SR Brandalise, OAC Clark, S Richards

Cochrane Database of Systematic Reviews 2007 Issue 1

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DOI: [10.1002/14651858.CD004139.pub2](https://doi.org/10.1002/14651858.CD004139.pub2) This version first published online: 20 July 2005 in Issue 3, 2005

Date of Most Recent Substantive Amendment: 20 April 2005

This record should be cited as: Sasse EC, Sasse AD, Brandalise SR, Clark OAC, Richards S. Colony stimulating factors for prevention of myelosuppressive therapy induced febrile neutropenia in children with acute lymphoblastic leukaemia. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD004139. DOI: [10.1002/14651858.CD004139.pub2](https://doi.org/10.1002/14651858.CD004139.pub2).






Abstract

Background

Acute lymphoblastic leukaemia (ALL) is the most common cancer in childhood and febrile neutropenia is a potentially life-threatening side effect of its treatment. Current treatment consists of supportive care plus antibiotics. Clinical trials have attempted to evaluate the use of colony-stimulating factors (CSF) as additional therapy to prevent febrile neutropenia in children with ALL. The individual trials do not show whether there is significant benefit or not. Systematic review provides the most reliable assessment and the best recommendations for practice.

Objectives

To evaluate the safety and effectiveness of the addition of G-CSF or GM-CSF to myelosuppressive chemotherapy in children with ALL, in an effort to prevent the development of febrile neutropenia. Evaluation of number of febrile neutropenia episodes, length to neutrophil count recovery, incidence and length of hospitalisation, number of infectious disease episodes, incidence and length of treatment delays, side effects (flu-like syndrome, bone pain and allergic reaction), relapse and overall mortality (death).





Search strategy

The search covered the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CANCERLIT, LILACS, and SciElo. We manually searched records of conference proceedings of ASCO and ASH from 1985 to 2003 as well as databases of ongoing trials. We consulted experts and scanned references from the relevant articles.

Selection criteria


We looked for randomised controlled trials (RCTs) comparing CSF with placebo or no treatment as primary or secondary prophylaxis to prevent febrile neutropenia in children with ALL.

Data collection and analysis

Two authors independently selected, critically appraised studies and extracted relevant data. The end points of interest were:

- * Primary end points: number of febrile neutropenia episodes and overall mortality (death)
- * Secondary end points: time to neutrophil count recovery, incidence and length of hospitalisation, number of infectious diseases episodes, incidence and length of treatment delays, side effects (flu-like syndrome, bone pain and allergic reaction) and relapse.

We conducted a meta-analysis of these end points and expressed the results as Peto odds ratios. For continuous outcomes we calculated a weighted mean difference and a standardised mean difference. For count data, meta-analysis of the logarithms of the rate ratios using generic inverse variance was employed.



Main results

We scanned more than 5500 citations and included six studies with a total of 332 participants in the analysis. There were insufficient data to assess the effect on survival. The use of CSF significantly reduced the number of episodes of febrile neutropenia episodes (Rate Ratio = 0.63; 95% confidence interval (CI) 0.46 to 0.85; $p = 0.003$, with substantial heterogeneity), the length of hospitalisation (weighted mean difference (WMD) = -1.58; 95% CI -3.00 to -0.15; $p = 0.03$), and number of infectious diseases episodes (Rate Ratio=0.44; 95%CI 0.24 to 0.80; $p=0.002$). In spite of these results, CSF did not influence the length of episodes of neutropenia (WMD = -1.11; 95% CI -3.55 to 1.32; $p = 0.4$) or delays in chemotherapy courses (Rate Ratio=0.77; 95%CI 0.49 to 1.23; $p=0.28$).

Authors' conclusions

Children with ALL treated with CSF benefit from shorter hospitalisation and fewer infections. However, there was no evidence for a shortened duration of neutropenia nor fewer treatment delays, and no useful information about survival.

The role of CSF regarding febrile neutropenia episodes is still uncertain. Although current data shows statistical benefit for CSF use, substantial heterogeneity between included trials does not allow this conclusion.

Plain language summary

Prophylactic administration of colony-stimulating factors reduces hospital stay and risk of infections in children with acute lymphoblastic leukaemia

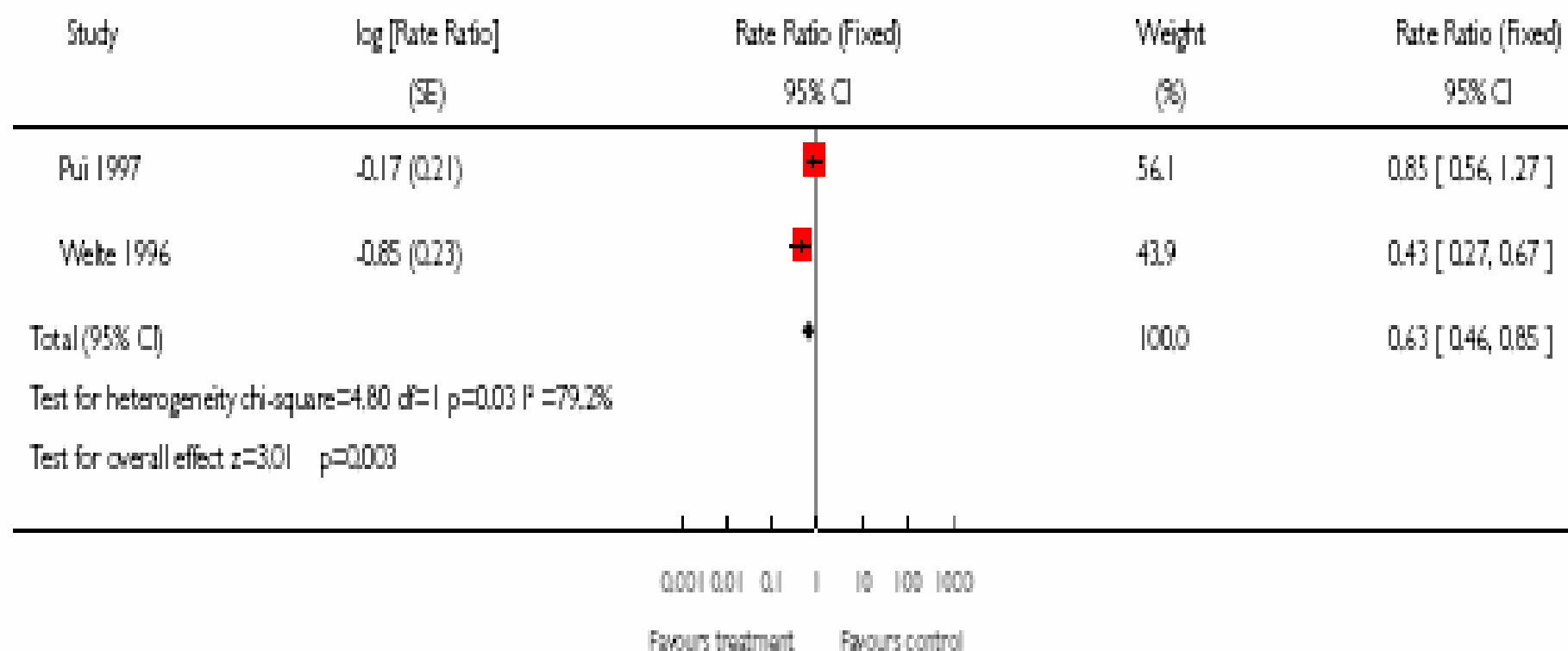
The authors evaluated the efficacy of adding colony-stimulating factors (CSF) after chemotherapy in children with acute lymphoblastic leukaemia (ALL) to prevent febrile neutropenia, which is an important life-threatening side effect of treatment. There is a lack of studies to determine the best CSF dose for children and the existence of only a small number of RCTs evaluating CSF role in children's ALL. The prophylactic administration of CSF reduces hospital stay, and risk of infections. The authors did not find evidence that CSF reduces either febrile neutropenia episodes or duration, and treatment delays in children with ALL undergoing chemotherapy. Follow-up was too short to provide useful information on any possible effect on relapse or survival.

Analysis 01.01. Comparison 01 Febrile neutropenia episodes, Outcome 01 Febrile neutropenia episodes

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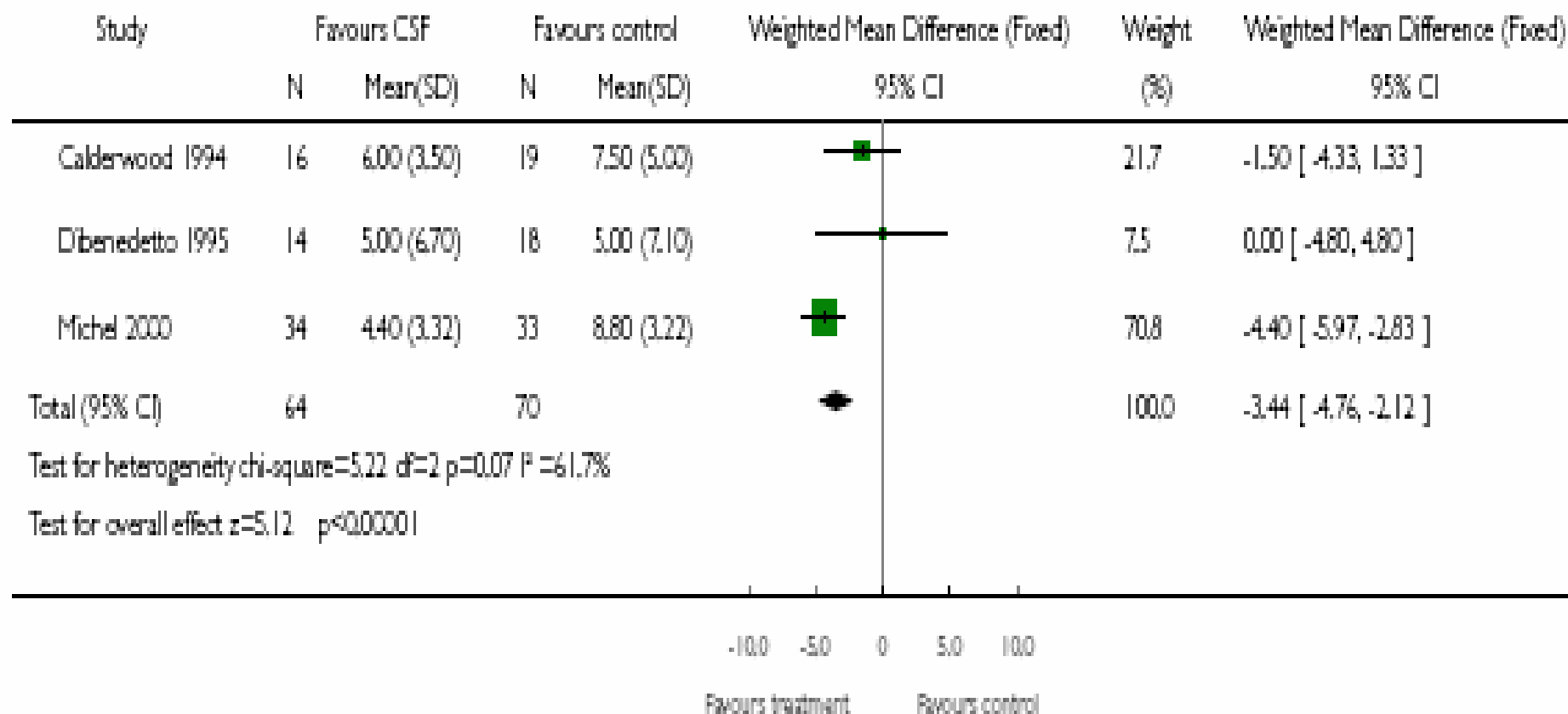


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Comparison: 02 Length of neutropenia

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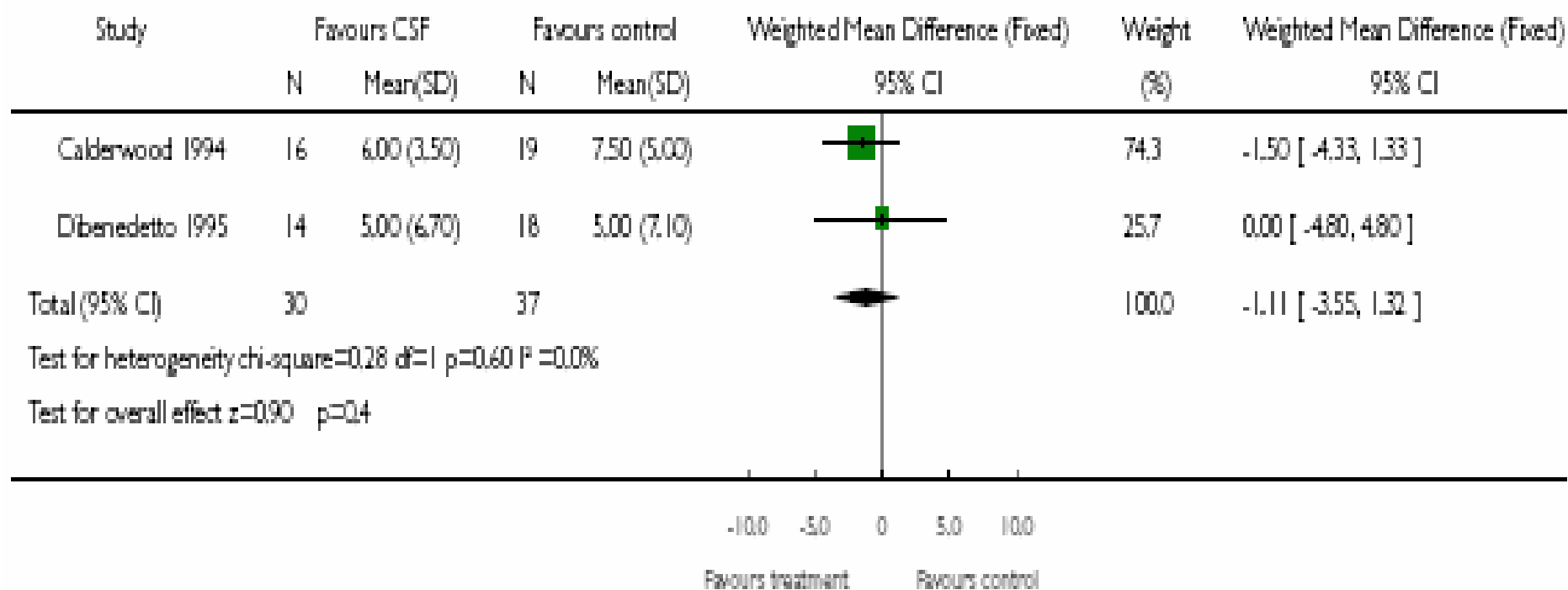


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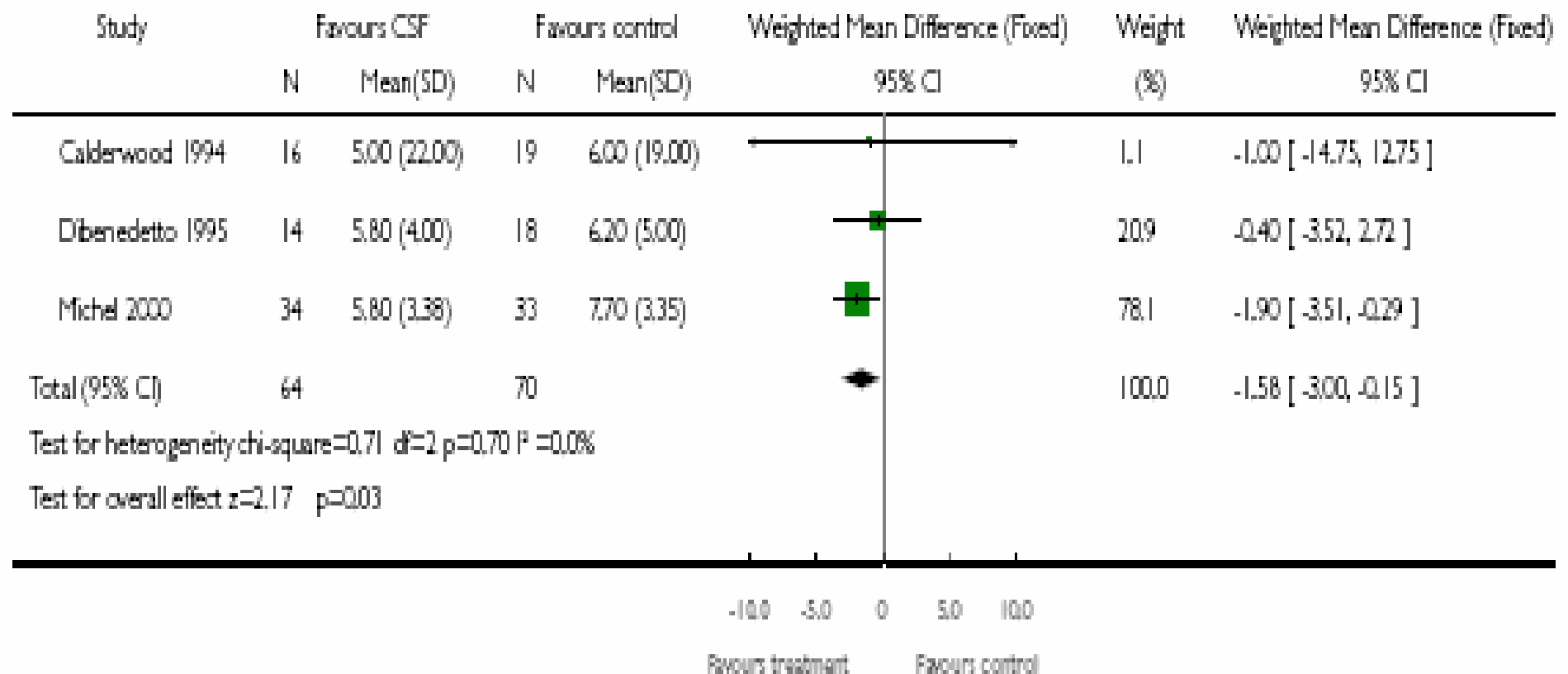


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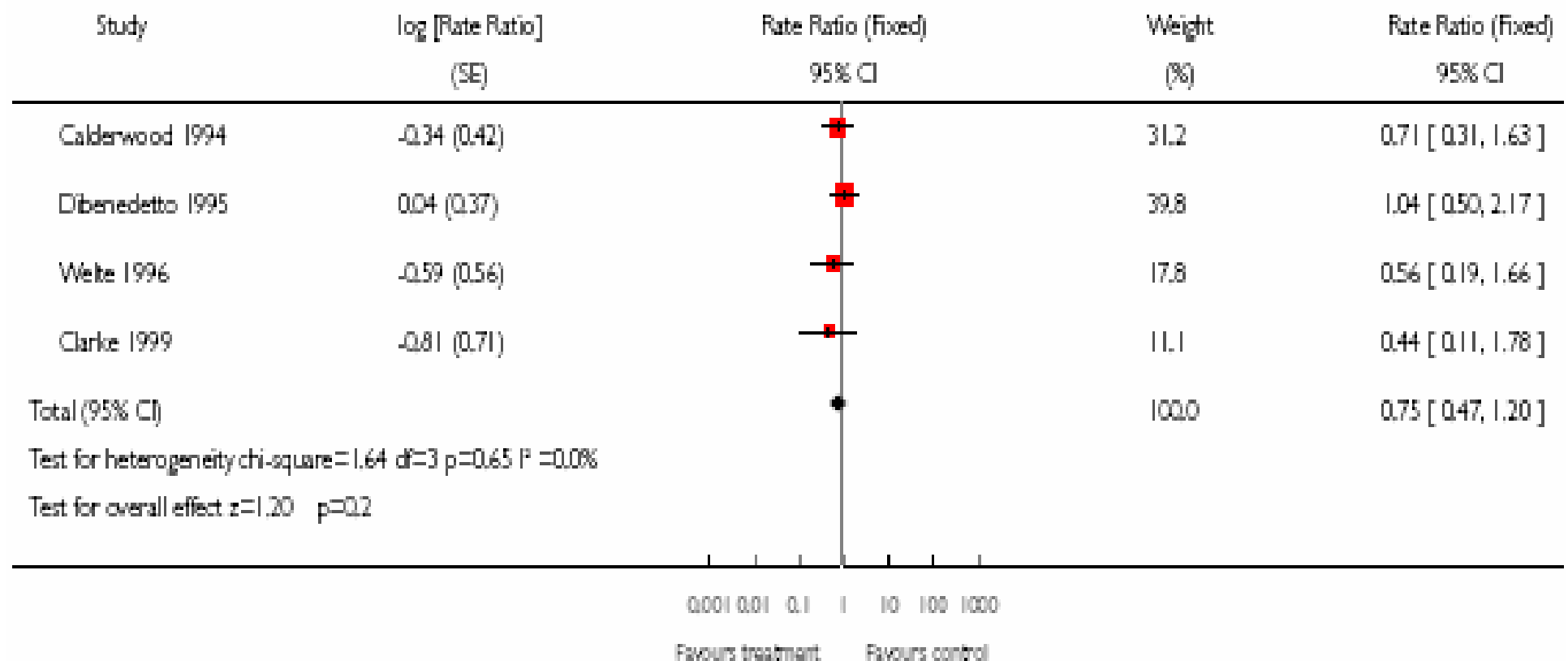


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Review: Colony stimulating factors for prevention of myelosuppressive therapy induced febrile neutropenia in children with acute lymphoblastic leukaemia

Comparison: 04 Delays in chemotherapy courses

Outcome: 01 Number of delays in chemotherapy

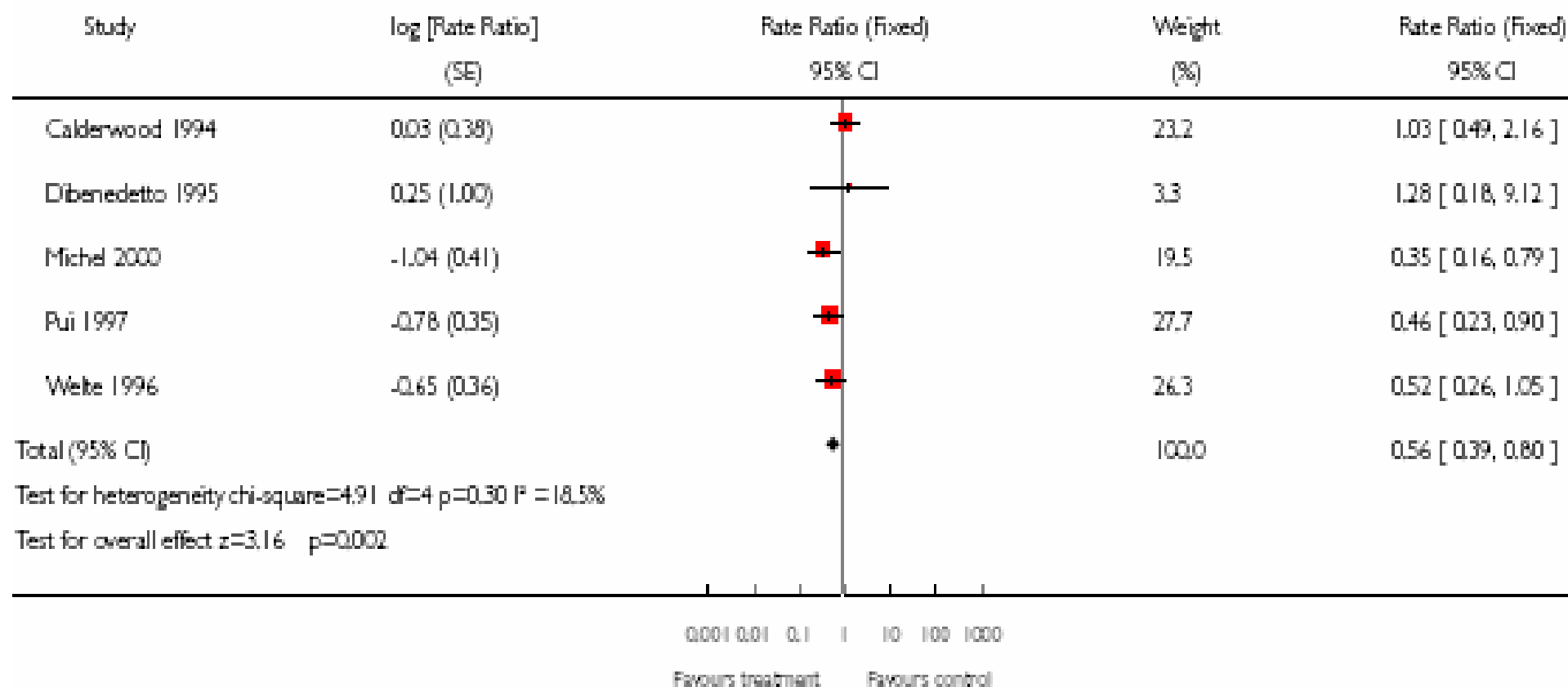


Analysis 05.01. Comparison 05 Number of infectious diseases episodes, Outcome 01 Number of infectious diseases episodes

Review: Colony stimulating factors for prevention of myelosuppressive therapy induced febrile neutropenia in children with acute lymphoblastic leukaemia

Comparison: 05 Number of infectious diseases episodes

Outcome: 01 Number of infectious diseases episodes





Critical Appraising for a Systemic Review

Are the Results Valid?

1. Did this review address a focused clinical question? **Yes**



2. Were the criteria for article inclusion appropriate ? **Yes**

RCTs with a parallel design that compare **CSF versus placebo or no treatment** given prior to the installation of neutropenia related to chemotherapy in children with ALL. **Children (0-18 years) with ALL receiving myelosuppressive chemotherapy**, excluding situations related to bone marrow transplantation.



3. Is it unlikely that relevant studies were missed? Not sure

4. Was the validity of the included studies appraised? **Yes**

5. Was the assessments of studies reproducible? **Yes**

6. Were the results similar from study to study?

similar : reduces length of hospitalisation



II What Are the Results?

1. What are the overall results of the review?

evidence :

reduces length of hospitalisation,
decreased the rate of infections during treatment

no evidence :

reduces the length of neutropenia episodes
diminishes delay of chemotherapy courses

1.fewer febrile neutropenia episodes in the CSF group,
substantial heterogeneity between trials prevents a
conclusion being drawn from this

2.no useful information is available on survival



III Will the Results Help Me In My Patient Care?

1. Can the results be applied to my patients ? **Yes**

2. Were all clinically important outcomes considered? **Yes**

3. Are the benefits worth the harms ?

Not done , no useful information is available on survival or relapse



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▶ **PREVENTION**

- Thionamides
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- Antineutrophil antibody assay

▶ **TABLES**

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- Drugs and agranulocytosis

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- ▶ Primary immune neutropenia
- ▶ Neutropenia associated with infections
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Drug-induced neutropenia and agranulocytosis

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INTRODUCTION — Most cases of neutropenia are acquired and are due to decreased gran production or, less often, increased destruction. Acquired neutropenia is most often due to accelerated turnover, usually resulting from immunologic mechanisms. ([See "Overview of ne" for an approach to the patient with neutropenia](#)).

On the other hand, with the exception of neutropenia following cytotoxic chemotherapy, dr induced neutropenia or agranulocytosis occurs as an idiosyncratic reaction. The usual defir drug-induced neutropenia or agranulocytosis excludes the use of known cytotoxic agents ([cyclophosphamide](#), [doxorubicin](#)) or diseases (eg, [vitamin B12](#) deficiency, chronic liver disease) can cause neutropenia, and requires that the drug has been administered within four week onset of neutropenia. Discontinuation of the drug generally results in correction of the neu count within 30 days.

This topic review will discuss drug-induced neutropenia and agranulocytosis. Others cause: acquired neutropenia, such as primary immune mechanisms, chemotherapy, and infections, discussed separately. ([See "Primary immune neutropenia"](#) and [see "Neutropenia associated w infections"](#) and [see "Prophylaxis of infection during chemotherapy-induced neutropenia"](#)).

DEFINITIONS — Neutropenia is defined as an absolute neutrophil count (ANC) of less than 1500/μL. The ANC is numerically equal to the product of the white blood cell count (W

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Prophylaxis of infection during chemotherapy-induced neutropenia

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INTRODUCTION — Intensive cytotoxic chemotherapy often causes profound neutropenia, which may result in hospitalization for treatment of fever or cause potentially fatal infection [1]. In an attempt to decrease infectious complications, recombinant human [granulocyte colony-stimulating factor](#) (G-CSF, [filgrastim](#)) and granulocyte-macrophage colony-stimulating factor (GM-CSF, [sargramostim](#)) have been used to reduce the duration and degree of neutropenia. Alternatively, prophylactic antibiotics have been administered to prevent the development of bacterial infection as a complication of the neutropenia.

The roles of the myeloid colony-stimulating factors (CSFs) and prophylactic antibiotics will be reviewed here. As will be seen, the data support use only in selected high-risk patients. The management of patients with chemotherapy-induced neutropenia and fever are discussed elsewhere ([See "Fever in the neutropenic adult patient with cancer"](#)).

DEFINITIONS

Neutropenia — Neutropenia is defined as an absolute neutrophil count (ANC) of less than 1500/microL. The ANC is equal to the product of the white blood cell count (WBC) and the fraction of polymorphonuclear cells (PMNs) and band forms:



COLONY STIMULATING FACTORS — CSFs have been evaluated for prophylactic use following the administration of chemotherapy when neutropenia is anticipated ("primary prophylaxis"), during retreatment after a previous cycle of chemotherapy that caused febrile neutropenia ("secondary prophylaxis"), and to shorten the duration of severe chemotherapy-induced neutropenia without fever ("afebrile neutropenia"). The use of CSFs has also been evaluated as an adjunct to other therapies in patients with febrile neutropenia. ([See "Fever in the neutropenic adult patient with cancer"](#)).

The likelihood of developing febrile neutropenia is the primary factor that determines whether or not prophylactic CSFs are indicated. The incidence of febrile neutropenia following treatment is influenced by the intensity of chemotherapy, the degree of injury to the gastrointestinal mucosa, the presence of underlying damage to the patient's hematopoietic stem cells, the concurrent use of radiation, and the overall clinical status of the patient (ie, age and comorbid conditions).

Primary prophylaxis


Indications and guidelines — Primary prophylaxis may be used to decrease the incidence of febrile neutropenia and the need for hospitalization. Primary prophylaxis may also be used to maintain dose-dense or dose-intense chemotherapy strategies that have survival benefits or if reductions in chemotherapy dose-intensity or dose-density are known to be associated with a poorer prognosis.

We recommend against the routine administration of myeloid CSFs for primary prophylaxis in previously untreated patients receiving chemotherapy regimens with a low probability of causing febrile neutropenia.

The 2006 guidelines from both the American Society of Clinical Oncology (ASCO) and the European Organization for Research and Treatment of Cancer (EORTC) recommend primary prophylaxis when the anticipated incidence of febrile neutropenia is approximately 20 percent or more [2,3]. Previous guidelines had recommended a cut-off of 40 percent [4]. The change in recommendation was driven by later randomized trials showing the cost effectiveness of this approach in patients with a risk of febrile neutropenia of approximately 20 percent [5,6].

There is strong evidence from multiple randomized trials that supports the use of CSFs to reduce the frequency of hospitalization for antibiotic therapy, even though this does not have a major effect on overall survival [6-9]. In a meta-analysis that included 1144 patients treated in eight randomized controlled trials, the average risk of febrile neutropenia was 51 percent in controls [10]. Prophylactic G-CSF resulted in a 62 percent reduction in the risk of febrile neutropenia (odds ratio [OR] 0.38, 95% CI 0.29-0.49) and a decrease in the incidence of documented infection (OR 0.51, 95% CI, 0.36-0.73); there was only a nonsignificant trend toward reduced infection-related mortality (OR 0.60, 95% CI, 0.3-1.22). The potential benefit of primary prophylaxis in children is less clear [11].





Primary prophylaxis with CSFs is also appropriate in a number of additional clinical settings [2,3]:

- Primary prophylaxis may also be indicated in patients who are being treated with curative intent to avoid reductions in dose-intensity or dose-density due to myelotoxicity (eg, lymphoma, adjuvant treatment for breast cancer, testicular cancer) [12-14]. This was illustrated in a controlled trial in which 80 patients with high-grade non-Hodgkin's lymphoma were randomly assigned to receive VAPEC-B chemotherapy alone or with daily G-CSF [12]. The use of G-CSF was associated with less grade 4 neutropenia (37 versus 85 percent), less febrile neutropenia (22 versus 44 percent), and a lesser likelihood of requiring chemotherapy dose reduction (10 versus 33 percent).
- High-risk patients who are treated with less myelosuppressive regimens may also benefit from prophylactic CSFs. This includes those with preexisting neutropenia, more advanced cancer, poor performance status, or, in the case of epithelial ovarian cancer, extensive prechemotherapy surgery, particularly if it included a bowel resection [15]. (See "[First-line chemotherapy for epithelial ovarian cancer](#)" and see "[Initial surgical management and follow-up of epithelial ovarian cancer](#)").
- For patients receiving radiation therapy involving large fields but not chemotherapy, therapeutic use of CSFs may be considered if prolonged delays secondary to neutropenia are expected.

Concomitant chemotherapy and radiation — In some solid tumors, chemotherapy and radiation are used to increase local control and survival [16,17]. Combined modality treatment also increases the incidence of febrile neutropenia, compared to radiotherapy alone [16,17].

However, GM-CSF has been associated with a higher incidence of thrombocytopenia and other complications when given with concurrent chemoradiotherapy. This was illustrated in a Southwest Oncology Group trial in which 215 patients with small cell lung cancer were randomly assigned to receive concurrent chemotherapy and thoracic radiotherapy with or without GM-CSF [18]. The incidence of grade 3 and 4 thrombocytopenia was significantly higher in the GM-CSF arm (91 versus 18 percent), and there were more treatment-related deaths among those receiving GM-CSF (9 versus 1, respectively).

This increase in toxicity may be specific to thoracic chemoradiotherapy and/or GM-CSF. Nonetheless, we suggest avoiding CSFs with combined modality therapy, outside a clinical trial setting.

Acute myeloid leukemia — The potential role of CSFs during induction therapy for acute myeloid leukemia is discussed elsewhere. (See "[Treatment of acute myeloid leukemia in adults](#)" and see "[Treatment of acute myeloid leukemia in older adults](#)").



Secondary prophylaxis — Secondary prophylaxis refers to the administration of a CSF in subsequent cycles after febrile neutropenia has occurred in a prior cycle. Secondary prophylaxis also includes the use of a CSF to speed recovery from neutropenia due to a previous cycle of chemotherapy, thus preventing delay in the administration of a subsequent chemotherapy cycle. The goal is to maintain chemotherapy dose intensity while avoiding dose reduction.

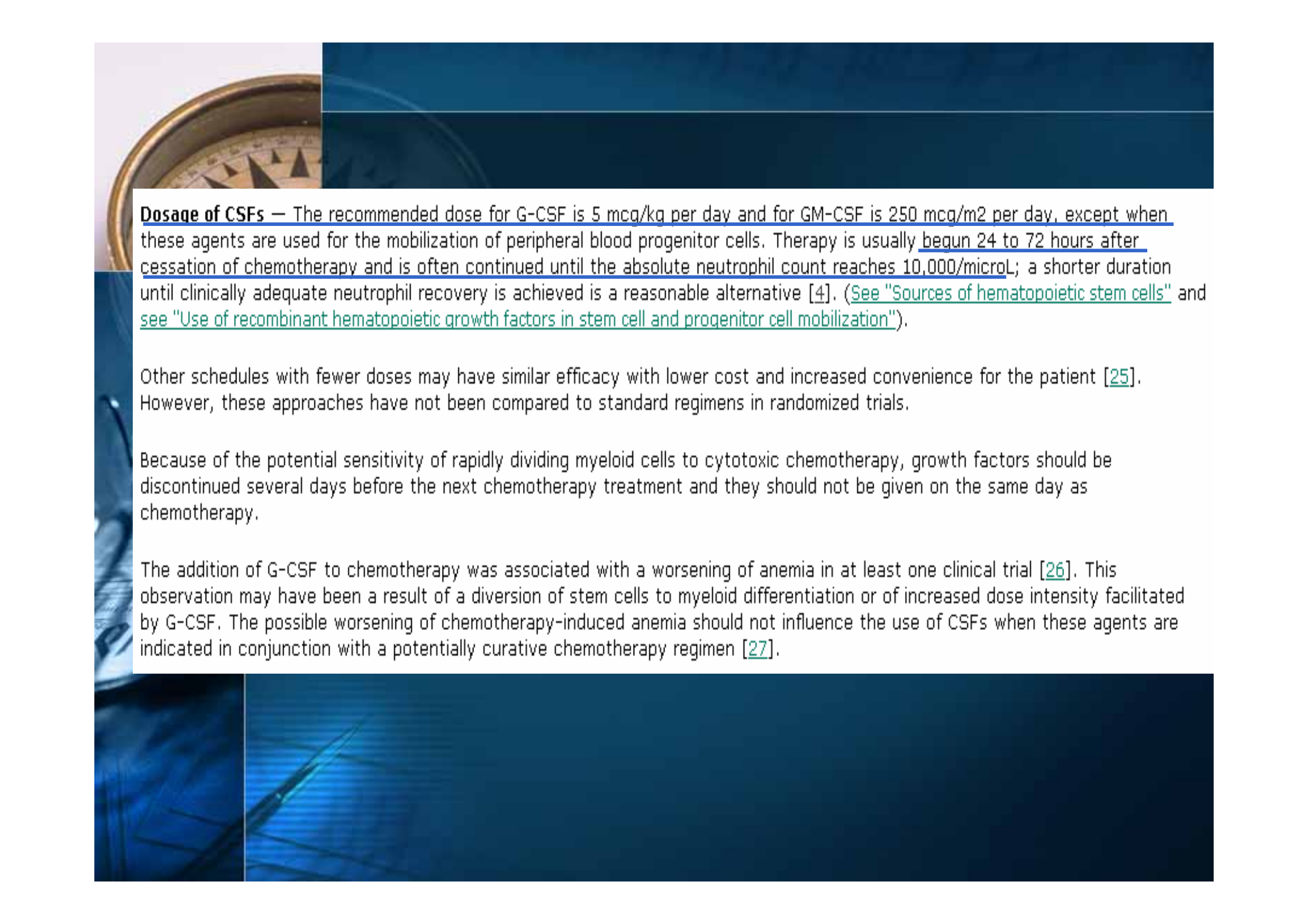
Dose reduction after an episode of severe neutropenia should be considered the primary therapeutic option, except when chemotherapy is being administered for the treatment of curable tumors (eg, germ cell cancer) [4]. No published regimen has shown improved disease-free or overall survival when secondary prophylaxis was instituted and the dose of chemotherapy was maintained.

Afebrile neutropenia — There is no established role for the use of CSFs in afebrile patients who have already developed severe neutropenia after chemotherapy. This was illustrated in a controlled trial in which 138 afebrile outpatients with severe chemotherapy-induced neutropenia (ANC \leq 500/microL) were randomly assigned to G-CSF or placebo until the ANC recovered to at least 500/microL [19]. The duration of severe neutropenia was modestly shorter with G-CSF (two versus four days), but there was no effect on the rate of hospitalization or number of culture-positive infections.

G-CSF versus GM-CSF — There are only limited data comparing G-CSF with GM-CSF. In one trial, 181 patients with chemotherapy-induced afebrile neutropenia (ANC \leq 500/microL) were randomly assigned to either G-CSF or GM-CSF [20]. Patients receiving G-CSF had a measurably shorter time to recovery from neutropenia, but the difference was not clinically meaningful [4]. In the absence of additional comparative data, there is no basis for recommending one CSF over the other for prophylaxis of infection during chemotherapy-induced neutropenia.

Pegfilgrastim — [Pegfilgrastim](#), a pegylated formulation of G-CSF, has a prolonged half-life, permitting the administration of a single dose rather than daily administration. The recommended dose (6 mg) is given 24 hours after chemotherapy, with at least 14 days elapsing until the next planned chemotherapy dose. Because of the altered pharmacokinetics, pegfilgrastim also has been used on a weekly basis, in conjunction with chemotherapy [21].

At least three randomized trials have shown that [pegfilgrastim](#) is as effective as and more convenient to administer than G-CSF for primary prophylaxis in patients requiring CSF treatment during myelosuppressive chemotherapy [22-24]. In the largest of these trials, 310 women with high-risk breast cancer receiving four courses of adjuvant [docetaxel](#) and [doxorubicin](#) every three weeks were assigned randomly to a single fixed dose of pegfilgrastim (100 mcg/kg) on day two of each cycle, or G-CSF (5 mcg/kg per day for 14 days or until the ANC was \geq 10,000/microL) [23]. The severity and duration of neutropenia and the side effect profile were similar in both groups.



Dosage of CSFs — The recommended dose for G-CSF is 5 mcg/kg per day and for GM-CSF is 250 mcg/m² per day, except when these agents are used for the mobilization of peripheral blood progenitor cells. Therapy is usually begun 24 to 72 hours after cessation of chemotherapy and is often continued until the absolute neutrophil count reaches 10,000/microL; a shorter duration until clinically adequate neutrophil recovery is achieved is a reasonable alternative [4]. (See "[Sources of hematopoietic stem cells](#)" and see "[Use of recombinant hematopoietic growth factors in stem cell and progenitor cell mobilization](#)").

Other schedules with fewer doses may have similar efficacy with lower cost and increased convenience for the patient [25]. However, these approaches have not been compared to standard regimens in randomized trials.

Because of the potential sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy, growth factors should be discontinued several days before the next chemotherapy treatment and they should not be given on the same day as chemotherapy.

The addition of G-CSF to chemotherapy was associated with a worsening of anemia in at least one clinical trial [26]. This observation may have been a result of a diversion of stem cells to myeloid differentiation or of increased dose intensity facilitated by G-CSF. The possible worsening of chemotherapy-induced anemia should not influence the use of CSFs when these agents are indicated in conjunction with a potentially curative chemotherapy regimen [27].



The conclusion

☐ For our patient :

1. ALL with TPOG-ALL-2002 SR reinduction chemotherapy
2. neutropenic fever episode
3. delayed next time chemotherapy

Prophylactic using of colony-stimulating factors is not recommended .



Thanks for your attention !!