**Human granulocyte colony-stimulating factor after induction chemotherapy in children with acute lymphoblastic leukemia**


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**Record Status**
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

**Health technology**
Use of granulocyte colony-stimulating factor (G-CSF)(10 micrograms per kg of body weight per day subcutaneously) for 15 days or until the postnadir neutrophil count was 1000 per cubic millimetre or higher for 2 days, after myelosuppressive remission-induction therapy in children and adolescents with acute lymphoblastic leukemia.

**Type of intervention**
Treatment and secondary prevention.

**Economic study type**
Cost-effectiveness analysis.

**Study population**
Children and adolescents with acute lymphoblastic leukemia undergoing a complete course of myelosuppressive remission-induction therapy.

**Setting**
Hospital. The economic study was carried out in the USA.

**Dates to which data relate**
Effectiveness and resource use data corresponded to those patients treated between December 1991 and August 1994. The price year was not explicitly specified.

**Source of effectiveness data**
Effectiveness data were derived from a single study.

**Link between effectiveness and cost data**
Costing was prospectively performed on the same patient sample as that used in the effectiveness analysis.

**Study sample**
Power calculations were used to determine the sample size (based on two other trials in the study institution with 399 similarly treated patients. The study sample was selected to detect a 20% reduction (from 40% to 20%) in the rate of hospitalisation with a power of 80% and alpha=0.05). The total number of eligible patients for randomization was 164 out of 167 (age range: 2 months - 17 years); 84 were randomly allocated to the placebo group and 80 to the G-CSF group. The total number of assessable patients remaining in the study after the exclusion of 7 patients in the G-CSF group and 9 in the placebo group (because of hospitalisation for parenteral antibiotic treatment at the time of pre-
planned initiation of the growth factor therapy) was 148; 73 in the G-CSF group with a median age of 5.8 (range: 0.2-17.9) years and 75 in the placebo group with a median age of 5.7 (range: 1.0-16.9) years.

**Study design**
Randomized, double-blind, placebo-controlled trial, carried out in a single centre. The duration of follow-up was 21 days (the likelihood of event-free survival was estimated at three years). There was no loss to follow-up. Stratification of patients was performed in terms of age, leukocyte count, and DNA index. The stratified randomisation was carried out one day (day 30) after the completion of remission-induction therapy.

**Analysis of effectiveness**
The principle used in the analysis of effectiveness was intention to treat. The primary end point of the study was the rate of hospitalisation for febrile neutropenia. The other clinical outcomes reported were the likelihood of event-free survival at three years, overall number of infections and severe infections. The patient groups were found to have comparable clinical features at the time of the diagnosis and at the initiation of the G-CSF therapy.

**Effectiveness results**
The rate of hospitalisation for febrile neutropenia was 58% in the G-CSF group versus 68% in the placebo group; (p=0.23); relative risk for the G-CSF group, 0.85; (95% CI: 0.59 - 1.16). The likelihood of event-free survival at three years was 83% in both study groups. The G-CSF group experienced 12 cases of overall infections versus 27 in the placebo group (p=0.009). The number of severe infections was 5 in the G-CSF group versus 6 in the placebo group (NS).

**Clinical conclusions**
The authors "found that G-CSF therapy, as compared with placebo, accelerated the recovery from neutropenia after myelosuppressive remission-induction therapy in children and adolescents with acute lymphoblastic leukemia but did not result in a decreased rate of hospitalization for febrile neutropenia, (or) a higher probability of event-free survival”.

**Measure of benefits used in the economic analysis**
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported.

**Direct costs**
Costs were not discounted due to the short time frame of the study. Quantities were reported separately from the costs. Some cost items were reported separately. The cost analysis covered the costs of intravenous antibiotics, transfusions, hospitalisations, and G-CSF. The perspective adopted in the cost analysis was not explicitly specified. The source of cost data was the study institution or official reports. The date of the price data was not explicitly specified.

**Statistical analysis of costs**
The costs of supportive care between the two study groups were compared using a Wilcoxon rank sum test.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).
Sensitivity analysis
A one-way sensitivity analysis was performed on the effect of lower dose of G-CSF on the cost of supportive care.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The G-CSF group had an estimated median cost of $8,768 (range: $1,435 - $79,674) versus $8,616 (range: $0 - $55,830) in the placebo group (p=0.83). The extra median cost of G-CSF was $1,845 (range: $1,435 - $2,665).

Synthesis of costs and benefits
Not combined.

Authors' conclusions
G-CSF treatment had some clinical benefit in children who received induction chemotherapy for acute lymphoblastic leukemia, but it did not reduce the rate of hospitalisation for febrile neutropenia, prolong survival, or reduce the cost of supportive care.

CRD COMMENTARY - Selection of comparators
The reason for the choice of placebo as the comparator is clear.

Validity of estimate of measure of benefit
The effectiveness results are likely to be internally valid due to the randomised double blind design adopted in the study. The study was a cost-consequences analysis.

Validity of estimate of costs
Quantities were reported separately from the costs. Some details of methods of cost estimation were not provided. The cost results may not be generalisable to other settings or countries.

Other issues
The authors' conclusions appear to be justified. The issue of generalisability to other settings or countries was not addressed, although, appropriate comparisons were made with other studies.

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Bibliographic details

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