A randomised study of prophylactic G-CSF following MRC UKALL XI intensification regimen in childhood ALL and T-NHL


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
The use of prophylactic granulocyte-colony stimulating factor (G-CSF), administered by subcutaneous injection following chemotherapy. The dose of G-CSF (Filgrastim) used was 5 microg/kg body weight.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The eligible patients were less than 17 years old and received chemotherapy according to the MRC ALL 97, UKALL XI or UKCCG 9504 NHL protocols.

Setting
The setting was tertiary care. The economic analysis was carried out in the UK.

Dates to which data relate
The effectiveness and resource use evidence was derived from a trial undertaken between 1996 and 1997. The price year was not stated.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The paper did not state how the costs were calculated. However, it appears that the resource use was obtained from a prospective costing carried out on the same sample of patients as that used in the effectiveness analysis.

Study sample
No power calculations to determine the sample size were reported. Forty-eight of the 89 eligible patients were recruited to the study, which was conducted at two paediatric cancer centres in the UK. The baseline characteristics of the sample were reported, and they appear to have been appropriate for the study question. Of the 41 (46%) patients who did not participate, 12 did so because of the trauma of the injections, 3 were unable to give informed consent, 21 were not approached, and 5 did not give reasons. Twenty-four patients were randomised to each crossover group.
Study design
This was a randomised crossover study carried out in two study centres. The patients were randomised "via a computer-generated system" to receive prophylaxis after one of two intensive chemotherapy blocks, at weeks 5 or 20. A crossover design was used so that patients receiving no treatment after the first block would receive G-CSF after the second block, and vice versa. The follow-up was for 28 days after commencing either the week 5 or week 20 chemotherapy block. Patients in either arm who were admitted to hospital with febrile neutropenia were treated with G-CSF at 5 microg/kg per day. Two (4%) of the 48 patients withdrew from the study before completion. The study was not blinded.

Analysis of effectiveness
The analysis of the clinical study was conducted on the basis of treatment completers only. The primary health outcome used was the rate of readmission for the treatment of febrile neutropenia. The patient characteristics were presented in order to compare diagnosis, gender and age between the groups. No adjustments were made for confounding factors. The authors stated that the numbers were too small to detect differences between the study groups.

Effectiveness results
Of the 46 patients receiving G-CSF, 34 (74%) required readmission to hospital for febrile neutropenia, compared with 42 (91%) of the 46 controls, (p=0.0386).

The duration of readmission was approximately 6 days for each group, with no evidence of any period effect.

Clinical conclusions
Prophylactic administration of G-CSF, following intensive therapy for the treatment of childhood ALL and T-NHL, significantly reduced the rate of readmission to hospital for the treatment of febrile neutropenia.

Measure of benefits used in the economic analysis
The outcome measure was that presented in the 'Effectiveness Results' section, viz., the reduction in the readmission rate to hospital. This was perceived as an advantage to both the child and family.

Direct costs
No discounting was carried out since the time scale was less than one year. The resource quantities and the unit costs were not presented or analysed separately. The costs measured were for G-CSF, outpatient drug administration, inpatient bed use, and antibiotics. The perspective was that of the hospital health care provider. The quantities were estimated from actual trial data. The source of the unit cost data was not recorded.

Statistical analysis of costs
Only point estimates of the average total costs were presented. No statistical analysis of the costs was carried out.

Indirect Costs
No indirect costs were included.

Currency
UK pounds sterling (£), and also US dollars ($). The conversion rate was 1.00 = $1.60.

Sensitivity analysis
No sensitivity analysis was carried out.
Estimated benefits used in the economic analysis
The benefits were reported in the 'Effectiveness Results' section.

Cost results
The total cost for the 46 patients was 138,246 when in the control group and 150,048 when in the G-CSF group. The authors stated that there was no significant difference in the costs. In addition, that therapy administered at home by the parents would produce a modest but not significant reduction in the total costs. Statistical tests of difference were not recorded.

Synthesis of costs and benefits
There was no synthesis of the costs and benefits.

Authors' conclusions
Prophylactic granulocyte-colony stimulating factor (G-CSF) can reduce readmission to hospital after UKALL intensification, but there is unlikely to be a cost-saving.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was explicit. The user should decide if it is justified in their own setting.

Validity of estimate of measure of effectiveness
The analysis used a randomised trial that was appropriate for the analysis. The study sample may not have been representative of the population since there was a greater willingness to recruit to the study in one centre than the other. The treatments were not blinded, which could have led to bias. Readmission was justified by the authors as a measure of effectiveness, but it does not directly account for health outcome or quality of life.

Validity of estimate of measure of benefit
No summary measure of benefit was used. This limits the comparability of the results to other studies and other treatments.

Validity of estimate of costs
All the relevant categories of cost for the hospital provider appear to have been included. However, there are insufficient details to determine whether all the relevant costs within categories have been included. The resource use was not treated stochastically. Also, the lack of a sensitivity analysis limits the ability of the user to determine the degree of uncertainty surrounding the results. The price year was not reported.

Other issues
The authors compared their results with several other studies and made appropriate comparisons. They considered that other practitioners should consider local factors such as G-CSF cost, ease of home administration and potential acceptance, when considering how generalisable the treatment is to other settings.

The perspective was a narrow one, confined to the costs of the hospital. The follow-up was only one month. No synthesis of the costs and benefits was undertaken. Therefore, the study's usefulness as an economic evaluation is limited.

Implications of the study
The authors comment that G-CSF can reduce readmission rates, but whether this should be standard practice would
depend on local factors.

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