Low-dose filgrastim significantly enhances neutrophil recovery following autologous peripheral-blood stem-cell transplantation in patients with lymphoproliferative disorders: evidence for clinical and economic benefit


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
Low-dose filgrastim in post-peripheral blood stem-cell transplantation (PBSCT).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Male and female patients undergoing high-dose chemotherapy for lymphoproliferative disease. The median age was 49 years (range: 28 - 65). Patients had either multiple myeloma, non-Hodgkin's lymphoma or Hodgkin's disease.

Setting
The setting was a hospital in Nottingham, United Kingdom.

Dates to which data relate
Effectiveness data were extracted from patients entered in the study from January 1994 until January 1996. Resources used were calculated from the day of stem-cell reinfusion. Price data related to the period 1994 to 1996. No price year was stated.

Source of effectiveness data
Effectiveness data was taken from a single study.

Link between effectiveness and cost data
Costing was undertaken on the same patient sample but whether it was undertaken prospectively or retrospectively was not stated.

Study sample
38 patients were randomized; 19 patients received filgrastim and 19 received a placebo. The treatment and placebo groups were balanced for age, sex, diagnosis, previous treatment, and status of transplantation. Recruitment was confined to patients with greater than 2.5 x 10^6/kg CD34+ cells in the stem-cell harvest since the authors wanted to ensure that all patients received an optimal stem cell graft. Power calculations to determine the sample size were not reported.
Study design
Randomized double-blinded controlled trial. The study was performed in a single centre. Follow-up started from the first day after stem-cell reinfusion and continued until the absolute neutrophil count (ANC) was greater than 0.5 x 10^9/L. The loss to follow up was not stated.

Analysis of effectiveness
The basis for the analysis of the clinical study was not stated. The primary health outcomes considered were the recovery time, the number of febrile patients requiring antibiotics and length of hospital stay.

Effectiveness results
With respect to recovery time patients who received filgrastim achieved an ANC greater than 0.5 x 10^9/L on the tenth day post-transplant (median 10, range: 9 - 13) compared with the fourteenth day (median 14, range:9 - 19) for the placebo group (P<.001). The time to reach an ANC greater than 1 x 10^9/L was 12 (range: 9 - 14) versus 16 (range: 10 - 25) days (P<.002). The reduction in the duration of post-transplant hospital stay was statistically significant from a median of 16 days in the placebo group to a median of 13 days (P=.003). The total number of febrile patients who then required intravenous antibiotic therapy was lower in the filgrastim-treated group (68% versus 89%) but this was not statistically significant (P=.08).

Clinical conclusions
Low-dose filgrastim (50 micro.g/m^2) significantly accelerates neutrophil recovery post-transplant for lymphoproliferative disorders compared with placebo and significantly reduces the duration of hospital stay.

Measure of benefits used in the economic analysis
The primary health outcomes considered were the recovery time, the number of febrile patients requiring antibiotics and length of hospital stay.

Direct costs
Costs were calculated in the institution from the day of stem-cell reinfusion and based on the mean in-patient stay post-transplant and the mean cost of drugs and blood products administered before discharge. The price year was not specified. Only direct costs originating in the hospital were included. Discounting was not applied as the period of study was less than 1 year.

Indirect Costs
Not stated.

Currency
UK pounds Sterling ().
day post-transplant (median 10, range: 9 - 13) compared with the fourteenth day (median 14, range: 9 - 19) for the placebo group (P<.001). The time to reach an ANC greater than 1 x 10^9/L was 12 (range: 9 - 14) versus 16 (range: 10 - 25) days (P<.002). The reduction in the duration of post-transplant hospital stay was statistically significant from a median of 16 days in the placebo group to a median of 13 days (P=.003). The total number of febrile patients who then required intravenous antibiotic therapy was lower in the filgrastim-treated group (68% versus 89%) but this was not statistically significant (P=.08).

Cost results
The shortened in-patient stay reduced the cost per patient by 961. The reduced blood-product requirement of the filgrastim group also contributed to a cost saving of 160 per patient. Drug expenditure caused by filgrastim increased by 79 per patient. The total intervention and comparator cost per patient was 4,519 and 5,561 respectively. The total incremental savings per patient were 1,042. Costs were calculated from the day of stem-cell reinfusion and to the discharge.

Synthesis of costs and benefits
Not combined. However, as the intervention was more effective and also cost less than the placebo group it was the dominant strategy.

Authors' conclusions
Low-dose filgrastim significantly reduces neutrophil engraftment time post-PBSCT and also reduces in-patient stay and costs, which makes it economically viable for patients who are undergoing high-dose chemotherapy.

CRD COMMENTARY - Selection of comparators
The study design was appropriate since a placebo was used as a comparator in a double-blinded randomized trial. However the representativeness of the sample and the method of randomization are not clear.

Validity of estimate of benefits:
The parameters observed in the clinical analysis (number of febrile days or recovery time) imply some measure of quality of life that has not been considered. A cost-utility analysis would probably be the best way to assess the effectiveness of the treatment. Moreover, further studies and longer follow-up are required to assess the potential adverse effects of filgrastim.

Validity of estimate of costs
Only hospital costs were considered. The addition of negative indirect costs (for example, increase in the number of working days) would probably increase the potential savings and reinforce the analysis.

Implications of the study
Since the administration of low-dose filgrastim in patients with lymphoproliferative disorders results in a reduction in procedural cost it can be suggested that the use of filgrastim in clinical practice would contribute to an efficient use of health care resources.

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