Randomized trial of bone marrow versus lenograstim-primed blood cell allogeneic transplantation in patients with early-stage leukemia: a report from the Societe Francaise de Greffe de Moelle


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 lenograstim-primed allogeneic blood cell transplantation (BCT) versus allogeneic bone marrow transplantation (BMT) was studied. BCT was conducted using a daily subcutaneous administration of lenograstim at the dose of 10 microg/kg.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with early stage leukaemia. The inclusion criteria specified that the patients had to be aged less than 55 years old, and have acute leukaemia and be in the first or second complete remission or have chronic myeloid leukaemia and be in the first chronic phase. The patients also had to have an HLA-A-, HLA-B-, or HLA-DR-matched sibling donor aged at least 18 years, and satisfy the common clinical and biological criteria usually required to receive an allogeneic transplantation.

Setting
The setting was secondary care. The economic analysis was conducted in Marseilles, France.

Dates to which data relate
The effectiveness and resource data were prospectively collected between September 1996 and October 1998. The price year was 1998.

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

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study, except for three patients who had no available cost data at the time of the analysis. The costing was performed on 98 patients from the study sample.

Study sample
Power calculations to determine the sample size were performed. A total of 111 patients were included in the study and randomised to either the BCT or BMT intervention. Of these, 101 (91%) patients finally proceeded to transplantation, 48 in the BCT group and 52 in the BMT group.

**Study design**
The study was a multi-centre randomised trial that was conducted in 17 centres. A randomisation with stratification of the centre and diagnosis was performed. The duration of follow-up was 2 years after transplantation for the effectiveness analysis and data were collected every 30 days. The duration of follow-up was 6 months for the cost analysis.

**Analysis of effectiveness**
The analysis of the clinical study was conducted on the basis of treatment completers only. The primary health outcome used in the analysis was the time to reach unsupported platelet counts of greater than 25 x10^9 platelets/L. The secondary health outcomes were the time to reach 50 x10^9 platelets/L and the time to become independent from platelet transfusions, neutrophil recovery and the occurrence of acute and chronic graft-versus-host disease (GVHD).

Intention to treat analysis was used for survival, relapse and measures of leukaemia-free survival. Patients in the BCT and BMT groups were shown to be comparable at baseline in terms of their age (mean: 37.3 versus 36.5 years), gender (56% versus 52% male) and prognosis factors for GVHD.

**Effectiveness results**
Blood cell collection led to a higher number of CD34+ and CD3+ cells being collected than did bone marrow collection, (p<10^-6).

The platelet counts of patients in the BCT group reached 25 x10^9 platelets/L 8 days earlier than did those in the BMT group, (p<10^-4). This difference increased to 11 days for the end point of 50 x10^9 platelets/L, (p<10^-5). This, in turn, led to a shorter time period (12 versus 18 days) to reach platelet transfusion independence, (p<10^-4). It also to fewer platelet transfusions (3 versus 6) during the first 180 days after transplantation, (p=0.002).

The median time to reach a neutrophil count of 0.5 x10^9/L was 6 days shorter in the BCT group, (p<0.00001). The median time to reach a count of 1 x10^9 neutrophils/L was also shorter (by 7 days) in the BCT group, (p<0.00001).

The patients in the BCT group were discharged sooner than those in the BMT group, (p<0.03), and were not rehospitalised more often, (p<0.05).

Forty-three patients developed grade 2 or higher acute GVHD. There was no difference between the two groups, 44% for versus 42% for BMT). GVHD occurred more often in the BCT group (50%) than in the BCT group (28%), (p<0.03), and was more severe, (p<0.03).

With a median follow-up of 20 months (range: 6 - 35), nine patients (9%) relapsed at a median of 7 months (range: 2 - 17) after transplantation. There was no difference between the two groups.

Overall, 31 patients died at a median of 5 months (range: 0.5 - 19). There was no difference between the two groups.

Two-year overall survival and leukaemia free-survival probabilities reached 66% (range: 56 - 75) and 67% (range: 56 - 76), respectively. There was no statistical difference between the two groups.

**Clinical conclusions**
BCT led to a quicker neutrophil and platelet recovery than did BMT.

**Measure of benefits used in the economic analysis**
The authors did not develop a summary benefit measure. A cost-consequences analysis was therefore performed.
**Direct costs**
The direct medical costs for 98 patients were estimated for the first 180 days after transplantation. These considered the costs of hospitalisation and visits to the outpatient clinic, transfusions, drugs, conditioning regimen, laboratory tests, and additional tests related to infectious events and parenteral nutrition. The costs of hospitalisation and outpatient visits included the hotel, personnel and the depreciation of equipment. The costs of clinical units were derived from a detailed observation of all consumed resources in physical quantities. The unit costs were estimated using average 1998 French prices. The step-down method was used to calculate the overheads of the unit costs of hospitalisation and outpatient visits. The drug costs were the average purchasing prices in the French Regional Center for Cancer Research and Treatment. The transfusion costs referred to the direct government regulation. The laboratory tests were evaluated using the prices of medical technical acts, established at the national level. The costs and the quantities were not reported separately. Discounting was unnecessary.

**Statistical analysis of costs**
A statistical analysis of the costs was carried out, but the methods used were not reported.

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
Euros (Euro).

**Sensitivity analysis**
No sensitivity analysis was conducted.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
Patients treated with BCT presented a 6% decrease in the total mean cost of the first 180 days, Euro37,410 versus Euro44,531, (p=0.004). However, the graft collection costs were significantly higher, Euro2,740 versus Euro2,449, (p<0.001).

The overall difference was mainly a result of the lower room cost in the BCT group (Euro17,408) than in the BMT group (Euro21,759), (p=0.01).

The difference in the total mean cost between the two groups was emphasised by substantial decreases in the costs of platelet transfusion (Euro934 versus Euro1,887), (p=0.004), laboratory tests (Euro5,220 versus Euro5,832), (p=0.04), and drugs (Euro6,450 versus Euro7,403), (p=0.022).

**Synthesis of costs and benefits**
Not applicable.

**Authors’ conclusions**
Allogeneic blood cell transplantation (BCT) results in quicker haematologic recovery. The decrease in hospitalisation and transfusion requirements associated with this quicker haematologic recovery offset the increased costs of using granulocyte colony-stimulating factor for collection, leading to a significant decrease in the total costs.
CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator, BMT, was clear. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The estimate of effectiveness should have high internal validity given the use of a blind, randomised controlled trial. However, the sample size was small, suggesting a lack of power calculations. The study sample was representative of the study population. It is likely that some effectiveness outcomes were based on treatment completers only, whereas survival estimates were based on intention to treat. Thus, the findings may not be generalised to the whole population.

Validity of estimate of measure of benefit
The authors did not develop a summary benefit measure. A cost-consequences analysis was performed.

Validity of estimate of costs
The perspective adopted was unclear, but it is likely to have been that of the health care system. The quantities were not reported separately from the costs, although adequate details of the methods used to estimate the costs were given. Although, as the authors acknowledged, some of the costs (radiologic investigation, intensive care hospitalisation, and in relation to the donors’ time off from work) were underestimated, they were confident that the omissions did not alter the cost comparison.

Other issues
The generalisability of the results to other settings or countries was not addressed. Adequate comparisons were made with studies dealing with the same topic. The authors enrolled patients with early stage leukaemia and this was reflected in their conclusions. The authors highlighted the limitations of their study and do not appear to have reported the results selectively.

Implications of the study
The authors suggested that future studies will require larger populations and longer follow-up to assess the impact of chronic GVHD on outcome for both relapse and quality of life.

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