The clinical effectiveness and financial impact of utilizing peripheral blood progenitor cells as rescue therapy following autologous bone marrow transplant

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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
Using peripheral blood progenitor cells (PBPC) as supportive therapy after high-dose chemotherapy (HDC) and autoBMT for the treatment of metastatic breast cancer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with stage IV breast cancer who experienced either hormone-receptor negative disease or failure of hormonal therapy.

Setting
Hospital. The economic study was carried out in Chicago, USA.

Dates to which data relate
The effectiveness and charge data were taken from the hospital records corresponding to the period between June 1989 through September 1992. Resource utilisation data were not systematically reported. Dollar values were adjusted to mid-fiscal year 1992 prices.

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

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

Study sample
No power calculations were reported. The study sample consisted of 42 patients, sequentially treated and classified into Group A (16), Group B (11) and Group C (15). Patients in groups A and B received thiotepa at 250 mg/m² x 3 doses and cyclophosphamide at 60 mg/kg per day x two days. Group B patients received granulocyte colony-stimulating factor (G-CSF) after autoBMT. Patients in group C received a one-time dose of 600 mg/m² of thiotepa, a continuous infusion of cyclophosphamide of 6,000 mg/m², and carboplatin in place of cisplatin. Group C patients received PBPC transplant in addition to autoBMT and were given G-CSF after transplant. Two patients from group A and one from...
group B, died before 60 days post-autoBMT and were excluded from the clinical part of the analysis.

**Study design**
This was a retrospective cohort study, carried out in a single centre. The duration of follow-up was until 60 days post autoBMT or readmission. No loss to follow up was mentioned except for the death of 3 patients who were excluded from the clinical analysis. All patients were treated with HDC. Chemotherapy was given on an inpatient basis and consisted of cyclophosphamide (4 g/m² on day 1) and etoposide (1 g/m² on day 2). G-CSF of 10 micro g/kg per day was given. The median administration of G-CSF was 13 days, range 9 to 24 days. Following autoBMT, G-CSF was given at 20 micro g/kg per day until the neutrophil count reached 500/micro L. Antibiotic treatment was initiated when patients had fever higher than 38.3 degree C.

**Analysis of effectiveness**
The principle (intention to treat, or treatment completers only) used in the analysis of effectiveness was not explicitly specified. The clinical indicators were inpatient days after autoBMT (LOS), days receiving antibiotics (ABX), number of units of red blood cells transfused (RBC), number of units of platelets transfused (SDP), last day of red blood transfusion (DRBC), last day of platelet transfusion (DSDP), number of febrile days (temperature > 38.3 C) (TEMP), days until neutrophil engraftment (NEUT), and days until platelet engraftment (PLT). Patients groups were comparable in terms of the extent of disease and prior therapies.

**Effectiveness results**
LOS for group A, B, and C were 30, 29, and 18 days.
ABX for group A, B, and C were 30, 28, and 5 days.
RBC for group A, B, and C were 10, 9, and 4 units.
SDP for group A, B, and C were 19, 15, and 5 units.
DRBC for group A, B, and C were 26, 22, and 11 days.
DSDP for group A, B, and C were 25, 24, and 9 days.
TEMP for group A, B, and C were 19, 12, and 3 days.
NEUT for group A, B, and C were 17, 14, and 9 days.
PLT for group A, B, and C were 25, 25, and 10 days.

The differences between group A and B were not significant in any of the clinical indicators. The differences between group B and C were significant in all of the clinical indicators (p<0.001). The differences between group A and C were significant in all of the clinical indicators (p<0.0001). About one third of all patients required re-admission to the hospital due to neutropenic-related fever.

**Clinical conclusions**
An improvement in clinical indicators points towards decreased patient morbidity. The use of G-CSF and PBPC as support measures significantly improved patient outcome after autoBMT.

**Measure of benefits used in the economic analysis**
No summary benefit measure was identified in the cost analysis, and only separate clinical outcomes were reported.
**Direct costs**
Discounting of costs was not required because of the short follow-up of the study. Quantities were not reported separately from the costs. The cost items were reported separately. Total charge values were adjusted using institutional cost-to-charge ratios. The perspective adopted in the cost analysis was not explicitly reported. Total charge included pre-admission work-up through 60 days post autoBMT, blood products, pharmacy, laboratory, and room charges. The source of cost data was the financial records of the study hospital. Dollar values were adjusted to mid-year 1992 dollar values using price increases implemented during the period June 1989-September 1992.

**Statistical analysis of costs**
Initial results were analysed using univariate analysis. Due to the small samples size, significant differences found in the initial comparison of means were compared further by adjustment matrix of pairwise comparison. A two-tailed test with an alpha level equal to 0.05 was used. Median values, standard deviations, and p-values were used.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analysis was not carried out.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
Pre-admission work-up through 60 days post autoBMT totalled for groups A, B, and C: $96,098, $90,156 and $69,762, respectively. Of these the cost of blood products for each group was $10,591, $6,484 and $3,623; pharmacy costs were $57,915, $31,808, and $27,006; laboratory costs were $21,348, $16,585 and $13,818; and room costs were $36,524, $34,072, and $28,743, respectively. The differences between group A and B, B and C were not significant for any of the cost items. The differences between group A and C were significant in all of the cost items (p<0.002) except for pharmacy costs (p<0.28).

**Synthesis of costs and benefits**
A synthesis of costs and benefits was not required since the use of CSF and PBPC as support measures was the dominant strategy.

**Authors' conclusions**
The use of CSF and PBPC as support measures leads to statistically significant reduction in resource consumption in all categories except pharmacy costs. An improvement in clinical indicators also points toward decreased patient morbidity. Future efforts should focus on identifying admission. Additional cost reductions may be realised by greater utilisation of outpatient care, thereby further reducing room and total charges. The use of home care services of the autoBMT could also help to reduce the number of re-admissions.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator is clear.
Validity of estimate of measure of effectiveness
The internal validity of the estimates of effectiveness may be weakened by the lack of a randomised design and a small sample size. Further information on follow-up of patients could have been provided.

Validity of estimate of costs
Resource utilisation was not reported separately from the costs. However, adequate details of methods of cost estimation were given. The study lacked a prospective cost analysis.

Other issues
Given the lack of randomisation and sensitivity analysis, and the small sample size, the results may need to be treated with some caution. The issue of generalisability to other settings or countries was not addressed.

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