Are hematopoietic colony-stimulating factors useful in association with chemotherapy in the treatment of HIV-related non-Hodgkin's lymphomas?

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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 hematopoietic colony-stimulating factors (CSF) in addition to antineoplastic chemotherapy versus standard chemotherapy regimens (LNH 84 or CHVmp viscristine-Belo) without CSF in the treatment of patients with HIV-related non-Hodgkin's lymphoma (HIV-NHL).

Type of intervention
Secondary prevention; Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with HIV-NHL undergoing chemotherapy.

Setting
Hospital. The economic study was carried out in Aviano, Italy.

Dates to which data relate
The effectiveness and resource use data were mainly collected from 1989 to 1991 for the control group of chemotherapy without G-CSF, and from 1991 to 1992, for chemotherapy with G-CSF. The price year was not clearly reported.

Source of effectiveness data
Effectiveness data were derived from a single study (Tirelli and Vaccher, 1994).

Link between effectiveness and cost data
The costing was retrospectively undertaken on the same patient sample as that used in the effectiveness study.

Study sample
Power calculations were not used to determine the study size. 37 patients were included in the study of whom 19 received chemotherapy without G-CSF, and 18 received chemotherapy with G-CSF.

Study design
The study was a non-randomised trial with historical controls. The controls corresponded to consecutive patients
immediately before the intervention (G-CSF) became available in the single study clinic, whereas the intervention group was formed by consecutive patients treated since the introduction of the intervention. Patients were followed up until hospital discharge (after toxicity and infection resolution). Losses to follow-up were not reported.

**Analysis of effectiveness**

The principle used to analyse the data was not explicitly specified. The primary health outcome was toxicity as measured by event rate of febrile neutropenia, mean duration (in days) of nadir white blood cell (WBC), mean number of chemotherapy cycles and proportion of patients receiving full doses of chemotherapy, mean duration of delays between cycles, response rates, and mean (SD) toxicity-related days of hospitalisation. The groups were reported as comparable in terms of age, sex, performance status, p24 antigenaemia, prior zidovudine therapy, stage and histology of NHL and bone marrow involvement.

**Effectiveness results**

The intervention (chemotherapy plus G-CSF) group had a duration of nadir WBC of 8.4 days, whilst the control group (chemotherapy alone) had a corresponding figure of 10.8 days (p=0.006). Mean nadir in patients with a CD4 count ≥200 per mm³ was 1293 (+/− 143) in the intervention group and 410 (+/− 285) in the control groups, (p=0.009). When all patients with any CD4 count were considered, the difference was lower with p = 0.09. Mean duration of delays between cycles was 4 and 9 days for the intervention and control groups, respectively (p=0.01). The event rates for febrile neutropenia, number of culture-confirmed infections, the mean number of chemotherapy cycles, the proportion of patients who received full doses of chemotherapy, the complete response rates (69% and 67% for intervention and control, respectively), were comparable between groups. Moreover, the severity of infection in the control group was reported as higher (no additional details were given apart from almost all being bronco pulmonary infiltrates) than that for the intervention group. The mean number (SD) of toxicity-related days of hospitalisation was 6.4 (SD=9.1) for the intervention group versus 18.0 (13.2) for the control group (P= 0.003).

**Measure of benefits used in the economic analysis**

Toxicity avoided, as measured by decrease in mean duration (in days) of nadir white blood cell (WBC), mean number of chemotherapy cycles and mean duration of delays between cycles were the main benefit measures.

**Direct costs**

Most quantities of resource use were not reported. The cost of hospitalisation for toxicity and G-CSF were measured. The cost items were not reported separately. The perspective adopted was that of the hospital. The therapeutic procedures and prices (unit hospital costs) were reported as ‘unchanged’ during the study period (1989-1992). Thus, it seems that prices were included in the analysis without any inflationary adjustment.

**Statistical analysis of costs**

Mann-Whitney tests were applied in the comparison of the overall cost estimates, which were reported with standard deviations (SD).

**Indirect Costs**

Not considered.

**Currency**

US dollars ($).

**Sensitivity analysis**

No sensitivity analysis was reported.
Estimated benefits used in the economic analysis
The intervention (chemotherapy plus G-CSF) group had a duration of nadir WBC of 8.4 days, whilst the control group (chemotherapy alone) had 10.8 days (p=0.006). The mean nadir in patients with a CD4 count >=200 per mm3 was 1293 (+/- 143) in the intervention group and 410 (+/- 285) in the control group, (p=0.009). Mean duration of delays between cycles was 4 and 9 days for the intervention and control groups, respectively (p=0.01).

Cost results
The mean 'hospitalisation and G-CSF cost' per cycle (SD) was $2,282 (1,345) for the intervention group, whilst the control had a mean cost of $3,232 (2283), (p>0.05).

Synthesis of costs and benefits
Since the intervention turned out to be the dominant strategy, the costs and benefits were not combined.

Authors' conclusions
The authors concluded that, "The results of the study strongly support the primary use of CSF in patients with HIV-NHL treated with chemotherapy, in order to reduce the myelosuppression and its associated morbidity, although the response rate and survival are not influenced. Moreover, CSF may improve patients' quality of life by decreasing the frequency of hospital admissions and the number of days spent in the hospital for episodes of fever with neutropenia. In the HIV setting, the risk of an increased retroviral replication with GM-CSF should be considered and this factor employed only with a concomitant antiretroviral treatment". They therefore advise the use of G-CSF in that setting.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator is clear. This was defined as the standard chemotherapy without CSF.

Validity of estimate of measure of benefit
The validity of the study results may be open to question given the source of bias implicit in the retrospective nature of the study. In particular, clinically significant differences in patient management practices between the two periods involved in the study might be critical, as the authors themselves noted in the paper.

Validity of estimate of costs
The cost analysis lacked adequate details regarding the methodology used in the cost analysis, and few quantities of resource use were reported separately from the costs. The price year was not clearly reported.

Other issues
Although statistical tests for the results between the main strategies were carried out, the conclusions may not be fully justified, given the remaining uncertainties in the data. The issue of generalisability was not addressed. Overall, given the lack of randomisation and sensitivity analysis, the results may need to be treated with some caution.

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Bibliographic details
Other publications of related interest

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