Significance of a partial or slow response to front-line chemotherapy in the management of intermediate-grade or high-grade non-Hodgkin's lymphoma: a literature review

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Authors' objectives
To assess the outcome of non-Hodgkin's lymphoma (NHL) in patients who achieve an incomplete response to primary chemotherapy, and to determine whether salvage treatment with intensive combination chemotherapy, with or without autologous bone marrow transplant (ABMT), is successful in such patients.

Searching
The search was described as 'comprehensive', but the authors did not state which sources were searched, or how the search was performed.

Study selection
Study designs of evaluations included in the review
Any reports of treatment using combination chemotherapy; all appeared to be case series.

Specific interventions included in the review
Chemotherapeutic agents: various combinations of amsacrine, bleomycin, cisplatin, cytarabine, cyclophosphamide, dexamethasone, doxorubicin, etoposide, fluorouracil, ifosfamide, leucovorin, mechlorethamine, methotrexate, methyl-gag, prednisolone, procarbazine and vincristine. ABMT.

Participants included in the review
For the first part of the review, NHL patients who achieved only a partial response to front-line therapy; for the second and third parts, assessing salvage therapy for aggressive NHL, patients who had achieved a complete or partial response to front-line therapy and subsequently relapsed.

Outcomes assessed in the review
Survival duration was assessed.

How were decisions on the relevance of primary studies made?
All studies found reporting this type of treatment were included. No independent reviewer was involved.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined narratively and tables were presented.

How were differences between studies investigated?
The authors did not report any investigation of differences between the studies.
Results of the review
In the first part of the review, 22 studies were included with 1,208 patients, of whom 1,010 were evaluated. In the second part, reporting on salvage chemotherapy, 10 studies were included but the number of patients is unclear. In the third part, reporting on autologous bone marrow transplantation, 4 studies involving 134 patients were included.

Patients with intermediate and high-grade NHL who do not show a complete response to front-line chemotherapy have a poor prognosis. The median survival duration of partial responders in most of the reports is less than 15 months. These poor results are common to first-, second- and third-generation chemotherapy protocols. The results reported for intensive salvage therapy appear to be equally poor, except in 2 small non-randomised studies where patients with a partial response to first-line therapy were treated with salvage chemotherapy before disease progression. Intensive salvage chemotherapy followed by ABMT appears to produce ‘impressive results’, but the follow-up periods were only 12 to 49 months.

Authors’ conclusions
Patients with aggressive NHL who fail to show a rapid and complete response to front-line chemotherapy have a poor prognosis. Early introduction of dose-intensive chemotherapy before the development of progressive disease may benefit patients with a partial response and requires testing in randomised clinical trials. ABMT should be offered early to patients who experience a partial response to front-line chemotherapy.

CRD commentary
It would be difficult for a non-specialist to make sense of this review. The authors use a great range of acronyms, not only for the chemotherapy regimens, where they might be justified, but also for many other terms such as the disease name (NHL), partial and complete response (PR and CR) and disease-free survival. This adds to the confusion of an already confusing review. The discussion lacks organisation and the relevance of many points made is unclear. In addition, the review fails to consider patients included in some studies but not evaluated; this could seriously distort the outcome. However, in view of the dismal survival rates reported in most of these studies, the loss of some patients is not likely to alter the conclusions. Quality of life is not mentioned, but the fact that patients are reported to have died from toxic effects of the chemotherapy regimes reviewed suggests that some survivors may suffer severe adverse effects of treatment during the limited period of life left to them.

Implications of the review for practice and research
Repeated use of intensive chemotherapy after progression of NHL does not appear to enhance survival in those patients who fail to respond completely to initial chemotherapy, and should not be recommended.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.