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Allogeneic stem cell transplantation for lymphoma – can we cure more patients?

INVITERT KOMMENTAR

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Allogeneic stem cell transplantation is now safer, with higher survival rates and fewer complications, potentially making this treatment accessible to more patients.

In Norway, transplantation of haematopoietic stem cells from a donor is offered as part of the multi-regional treatment provision for allogeneic stem cell transplantation (ASCT) (1). This is available at two hospitals in Norway: Oslo University Hospital and Haukeland University Hospital in Bergen. The primary indications are cancer or bone marrow failure for which no other curative treatment is available.

Replacing a cancer patient's haematopoietic cells and immune system with cells from a healthy donor serves two purposes: enabling more intensive cancer treatment prior to transplant and facilitating the curative graft-versus-tumour effect. In this process, the donor's immune system, particularly the effector T cells, monitors and eliminates any remaining cancer cells. Unfortunately, the donor's T cells can also cause severe damage to the recipient's organs, manifesting as graft-versus-host disease (GVHD). This condition can significantly reduce the patient's survival prospects and quality of life. Transplanters must always balance the risk of GVHD against the risk of relapse, as measures to suppress one condition can potentially lead to the other.

The Norwegian Cancer Registry recorded 1274 cases of lymphoma in Norway in 2023. Survival rates are improving due to advancements in diagnostics and treatment. The five-year relative survival rate for non-Hodgkin's lymphoma is 77.3 % for men and 81.3 % for women, compared to 90.7 % and 88.4 % for Hodgkin's lymphoma (2).

> ***«The guidelines for ASCT in malignant lymphomas estimate a higher number of eligible patients than the number of transplants in recent years»***

Two medical specialties are responsible for lymphoma treatment in Norway. In general, patients eligible for high-dose therapy and advanced cell therapy should be referred to *lymphoma oncologists* at regional hospitals, while other patients can be treated at smaller hospitals under the care of a *haematologist*. Patients approved for ASCT undergo transplantation and receive post-transplant follow-up from haematologists as part of the multi-regional treatment provision.

Most patients with lymphoma do not meet the criteria for ASCT. However, the guidelines for ASCT in malignant lymphomas estimate a higher number of eligible patients than the number of transplants in recent years (3). Concerns about mortality associated with organ toxicity, infections and GVHD have likely contributed to the reduction in ASCTs. Reduced-intensity conditioning reduces toxicity and mortality and is preferrable to myeloablative regimens for lymphoma patients (4).

In the retrospective registry study published in this edition of the Journal of the Norwegian Medical Association, Frøen et al. compare data on lymphoma patient outcomes following transplantation at Oslo University Hospital before and after the introduction of antithymocyte globulin (ATG) for GVHD prophylaxis (5). The results are highly encouraging, showing a twofold increase in two-year survival without relapse or GVHD, along with a significant reduction in transplant-related mortality in the most recent five-year period following the introduction of ATG (group 2). The fall in chronic GVHD is particularly striking (39 % vs. 6 %). This supports previous findings in the field (6) and represents a very positive development. Furthermore, group 2 has more unrelated stem cell donors than group 1 and a lower median donor age (26 years vs. 41 years). Younger donors are associated with a higher likelihood of survival (7). Of the 120 patients, only three had undergone transplantation without reduced-intensity conditioning: two in group 1 and one in group 2. The choice of conditioning regimen does not therefore explain the differences in survival rates between the two groups.

> ***«The annual reports from the multi-regional treatment provision show an increase in the number of ASCTs for patients with lymphoma, from 5 in 2022 to 13 in 2023 and 15 in 2024»***

In October 2022, the Decision Forum for New Methods approved the introduction of treatment with CD19-targeted chimeric antigen receptor T-cells (CAR-T) for certain aggressive, chemotherapy-resistant lymphomas. A decrease in the number of transplants might have been expected after this, as has been observed internationally (8). However, the annual reports from the multi-regional treatment provision show an increase in the number of ASCTs for patients with lymphoma, from 5 in 2022 to 13 in 2023 and 15 in 2024 (9, 10).

Access to new medications as a bridge to transplantation, in addition to fewer observed transplant-related complications, may have contributed to more patients being offered ASCT, even after CAR-T treatment became available. Frøen et al.'s study demonstrates why ASCT still deserves to play a role in the treatment of lymphoma.

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