# Hematopoietic Stem Cell Transplantation for Non-Hodgkin Lymphoma

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**KEYWORDS**

- Non-Hodgkin lymphoma • Diffuse large B-cell lymphoma • Follicular lymphoma
- Mantle cell lymphoma • Peripheral T-cell lymphoma
- Autologous hematopoietic stem cell transplantation
- Allogeneic hematopoietic stem cell transplantation

**KEY POINTS**

- Autologous stem cell transplantation can improve survival in primary refractory or relapsed aggressive B-cell lymphoma and mantle cell lymphoma as well as in relapsed follicular or peripheral T-cell lymphoma.
- Autologous stem cell transplantation in first remission in selected patients with high-risk aggressive B-cell lymphoma, mantle cell lymphoma, and peripheral T-cell lymphoma is associated with improved progression-free survival.
- Allogeneic stem cell transplantation offers a lower relapse rate but a higher nonrelapse mortality resulting in overall survival similar to autologous stem cell transplantation.
- Allogeneic stem cell transplantation can be considered in select patients who fail induction therapy, autologous stem cell transplantation, or are ineligible for autologous transplant.

## INTRODUCTION

With the lifetime probability of developing non-Hodgkin lymphoma (NHL) of approximately 2%, NHL is a leading cause of cancer with an estimated 70,800 new diagnoses in the United States in 2014. Although the 5-year survival of NHL has improved from 47% (1975–1977) to 71% (2003–2009) in the last 3 decades, NHL is estimated to account for 18,990 deaths in the United States in 2014.[1] This finding highlights a need for an improvement in up-front and salvage therapy for NHL. Hematopoietic stem cell transplantation (SCT) is a therapeutic option, which may offer a survival benefit to select patients, as described later.

Conflict of interest: The authors have nothing to disclose.
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## PATIENT EVALUATION OVERVIEW

A multidisciplinary approach to patient selection may reduce transplant-related mortality (TRM) and morbidity (Table 1). Hematopoietic cell transplantation comorbidity index (HCT CI) predicts nonrelapse mortality (NRM) and survival in allogeneic SCT (alloSCT) for hematologic malignancy[2] as well as autologous SCT (autoSCT) for lymphoma.[3] HCT CI is more sensitive and has a better survival prediction than the Charlson Comorbidity Index. Additionally, elevated lactate dehydrogenase (LDH) and the absence of chemosensitivity also predict higher NRM.[2,3] Patients who are older than 60 years are frequently not considered good candidates for myeloablative alloSCT but may be eligible for nonmyeloablative alloSCT. The presence of human immunodeficiency virus (HIV) or hepatitis B or C does not preclude autoSCT but may require further evaluation and close monitoring. The role of alloSCT in patients with HIV is currently not established.

## INDICATIONS OF TRANSPLANTATION

High-risk aggressive B-cell lymphoma, mantle cell lymphoma (MCL), relapsed or refractory B-cell lymphoma, and peripheral T-cell lymphoma (TCL) have poor overall survival (OS) with conventional chemotherapy and are candidates for high-dose chemotherapy (HDT) followed by autoSCT or alloSCT (Fig. 1, Table 2).

## TRANSPLANTATION IN AGGRESSIVE NON-HODGKIN LYMPHOMA

Diffuse large B-cell lymphoma (DLBCL) consisting of approximately one-third of all NHL is the most common aggressive NHL.[4] It can arise de novo or as a transformation of indolent lymphoma, such as follicular lymphoma (FL).[5] Although rituximab-based immunochemotherapy has improved OS in DLBCL, high-intermediate–risk or high-risk disease is associated with a 4-year OS of 49% to 59%.[6] SCT has been extensively investigated in both up-front and salvage settings.

### *Up-front Autologous Stem Cell Transplantation for Aggressive Non-Hodgkin Lymphoma*

Several trials have failed to show an OS benefit with up-front HDT/autoSCT in DLBCL or other aggressive NHL. A meta-analysis of 15 randomized controlled trials (n = 3079) highlighted a similar TRM ($P = .14$) and higher complete remission rate ($P = .004$) but no improvement in event-free survival (EFS) ($P = .31$) or OS ($P = .58$) with HDT/autoSCT,

**Table 1**
**Patient evaluation for hematopoietic SCT for NHL**

| Rational | Evaluation |
|---|---|
| Restaging of NHL | CT or PET scan, bone marrow and lymph node biopsies |
| Risk assessment for TRM | Performance status, nutritional and psychosocial status, viral serologies (particularly for alloSCT), cardiopulmonary, renal and liver function tests |
| Key eligibility criteria | Karnofsky performance score ≥70%, ejection fraction ≥40%, DLCO ≥50%, and serum creatinine clearance of ≥50 mL/min for autoSCT; also serum total bilirubin <2 times the upper limit of normal for alloSCT |

*Abbreviations:* alloSCT, allogeneic stem cell transplantation; autoSCT, autologous stem cell transplantation; CT, computed tomography; DLCO, diffusion capacity for carbon monoxide corrected for hemoglobin; PET, positron emission tomography.