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Medical Policy Hematopoietic Cell Transplantation for Non-Hodgkin Lymphomas

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Policy Number: 143

BCBSA Reference Number: 8.01.20 (For Plan internal use only)

Related Policies

- Hematopoietic Cell Transplantation for Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma, #<u>074</u>
- Hematopoietic Cell Transplantation for Hodgkin Lymphoma, #207
- Hematopoietic Cell Transplantation for Primary Amyloidosis, #181
- Hematopoietic Cell Transplantation for Waldenstrom's Macroglobulinemia, #322

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Non-Hodgkin's lymphoma (NHL)

For individuals with non-Hodgkin's lymphoma (NHL), B-cell subtypes considered aggressive (except mantle cell lymphoma), either allogeneic hematopoietic stem cell transplantation (HCT) using a myeloablative conditioning regimen or autologous HCT for the following indications may be considered MEDICALLY NECESSARY:

- As salvage therapy for individuals who do not achieve a complete remission (CR) after first-line treatment (induction) with a full course of standard-dose chemotherapy,
- To achieve or consolidate a CR for those in a chemosensitive first or subsequent relapse, or
- To consolidate a first CR in individuals with diffuse large B-cell lymphoma, with an adjusted International Prognostic Index score that predicts a high- or high-intermediate risk of relapse.

Mantle Cell Lymphoma

For individuals with mantle cell lymphoma:

- Autologous HCT to consolidate a first remission may be <u>MEDICALLY NECESSARY</u>.
- Allogeneic HCT, myeloablative or reduced-intensity conditioning, as salvage therapy may be <u>MEDICALLY NECESSARY</u>.
- Autologous HCT is considered **INVESTIGATIONAL** as salvage therapy.
- Allogeneic HCT is considered **INVESTIGATIONAL** to consolidate a first remission.

NHL B-cell Subtypes

For individuals with NHL B-cell subtypes considered indolent, either allogeneic HCT using a myeloablative conditioning regimen or autologous HCT for the following indications may be <u>MEDICALLY</u> <u>NECESSARY</u>:

- As salvage therapy for individuals who do not achieve CR after first-line treatment (induction) with a full course of standard-dose chemotherapy, or
- To achieve or consolidate CR for those in a first or subsequent chemosensitive relapse, whether or not their lymphoma has undergone transformation to a higher grade.

Either autologous HCT or allogeneic HCT is considered **INVESTIGATIONAL**:

- as initial therapy (ie, without a full course of standard-dose induction chemotherapy) for any NHL;
- to consolidate a first CR for individuals with diffuse large B-cell lymphoma and an International Prognostic Index score that predicts a low- or low-intermediate risk of relapse;
- to consolidate a first CR for those with indolent NHL B-cell subtypes.

T-cell or NK-cell (peripheral T-cell) Lymphoma

For individuals with mature T-cell or NK-cell (peripheral T-cell) lymphoma for the specified indications:

- Autologous HCT may be <u>MEDICALLY NECESSARY</u> to consolidate a first CR in high-risk peripheral T-cell lymphoma.
- Autologous or allogeneic HCT (myeloablative or reduced-intensity conditioning) may be <u>MEDICALLY</u> <u>NECESSARY</u> as salvage therapy.
- Allogeneic HCT is considered **INVESTIGATIONAL** to consolidate a first remission.

Hepatosplenic T-cell Lymphoma

For individuals with hepatosplenic T-cell lymphoma:

- Allogeneic HCT may be considered <u>MEDICALLY NECESSARY</u> to consolidate a first CR or partial response.
- Autologous HCT may be considered <u>MEDICALLY NECESSARY</u> to consolidate a first response if a suitable donor is not available or for individuals who are ineligible for allogeneic HCT.
- Autologous or allogeneic HCT as initial therapy (i.e., without a full course of standard-dose induction chemotherapy) is considered <u>INVESTIGATIONAL</u>.

Reduced-intensity conditioning allogeneic HCT as a treatment of NHL may be <u>MEDICALLY</u> <u>NECESSARY</u> in patients who meet criteria for an allogeneic HSCT but who do not qualify for a myeloablative allogeneic HCT.

Tandem transplants are considered **INVESTIGATIONAL** to treat patients with any stage, grade, or subtype of NHL.

Guidelines for use of bone marrow

Stem cells when harvested from the patient's bone marrow prior to marrow ablative therapy or from a donor's marrow after verifying the donor and recipient are well matched with respect to human leukocyte antigens (HLA) may be considered <u>MEDICALLY NECESSARY</u>. Verification of well-matched HLA donor and recipient is based on the attending or treating physician's clinical judgment.

Umbilical cord stem cell support as an acceptable cell source for transplants that are otherwise covered for either high-dose chemo with stem cell support, or for bone marrow transplant may be considered **MEDICALLY NECESSARY** when ALL the following are met:

1. Recipient is a child or adult, AND

- 2. There is no other available stem-cell donor with the same or better matching characteristics, AND
- 3. Donors may be related or unrelated.

Collection and storage of cord blood from neonate when an allogeneic transplant is "imminent" in an identified recipient with a diagnosis that is consistent with the possible need for allogeneic transplant may be considered **MEDICALLY NECESSARY**.

Exclusions:

- 1. Facility providing umbilical cord blood that is not in compliance with any existing FDA regulations governing umbilical cord transplants. FDA regulations are currently under development.
- 2. There is a suitable stem cell donor of equal or superior HLA match, and
- 3. Storage for future use, in case of a future need for transplant (prophylactic collection and storage).

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization <u>IS REQUIRED</u> for all products if the procedure is performed <u>inpatient</u>.
- Outpatient
- For services described in this policy, see below for products where prior authorization <u>might be</u> <u>required</u> if the procedure is performed <u>outpatient</u>.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is required .
Commercial PPO and Indemnity	Prior authorization is required .

Requesting Prior Authorization Using Authorization Manager

Providers will need to use <u>Authorization Manager</u> to submit initial authorization requests for services. Authorization Manager, available 24/7, is the quickest way to review authorization requirements, request authorizations, submit clinical documentation, check existing case status, and view/print the decision letter. For commercial members, the requests must meet medical policy guidelines.

To ensure the service request is processed accurately and quickly:

- Enter the facility's NPI or provider ID for where services are being performed.
- Enter the appropriate surgeon's NPI or provider ID as the servicing provider, *not* the billing group.

Authorization Manager Resources

Refer to our Authorization Manager page for tips, guides, and video demonstrations.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above <u>medical necessity criteria MUST</u> be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

CPT Codes

CPT codes:	Code Description
38240	Hematopoietic progenitor cell (HPC); allogeneic transplantation per donor
38241	Hematopoietic progenitor cell (HPC); autologous transplantation

HCPCS Codes

HCPCS	
codes:	Code Description
S2142	Cord blood derived stem-cell transplantation, allogeneic

S2150	Bone marrow or blood-derived peripheral stem-cell harvesting and transplantation,
	allogeneic or autologous, including pheresis, high-dose chemotherapy, and the
	number of days of post-transplant care in the global definition (including drugs;
	hospitalization; medical surgical, diagnostic and emergency services)

ICD-10 Procedure Codes

ICD-10-PCS	
codes:	Code Description
30233G0	Transfusion of Autologous Bone Marrow into Peripheral Vein, Percutaneous Approach
30233X0	Transfusion of Autologous Cord Blood Stem Cells into Peripheral Vein,
	Percutaneous Approach
20222V0	Transfusion of Autologous Hematopoietic Stem Cells into Peripheral Vein,
3023310	Percutaneous Approach
30243G0	Transfusion of Autologous Bone Marrow into Central Vein, Percutaneous Approach
30243X0	Transfusion of Autologous Cord Blood Stem Cells into Central Vein, Percutaneous
	Approach
30243Y0	Transfusion of Autologous Hematopoietic Stem Cells into Central Vein,
	Percutaneous Approach
3E03305	Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305	Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach
3E05305	Introduction of Other Antineoplastic into Peripheral Artery, Percutaneous Approach
3E06305	Introduction of Other Antineoplastic into Central Artery, Percutaneous Approach

Description

Treatment for Non-Hodgkin Lymphoma

Hematopoietic Cell Transplantation

Hematopoietic cell transplantation (HCT) is a procedure in which hematopoietic stem cells are intravenously infused to restore bone marrow and immune function in cancer patients who receive bone marrow-toxic doses of cytotoxic drugs with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allogeneic HCT [allo-HCT]). These cells can be harvested from bone marrow, peripheral blood, or the umbilical cord blood shortly after delivery of neonates. Cord blood transplantation is discussed in detail in policy #285.

Immunologic compatibility between infused hematopoietic stem cells and the recipient is not an issue in autologous HCT. In allogeneic stem cell transplantation, immunologic compatibility between donor and patient is a critical factor for achieving a successful outcome. Compatibility is established by typing human leukocyte antigens (HLA) using cellular, serologic, or molecular techniques. HLA refers to the gene complex expressed at the HLA-A, -B, and -DR (antigen-D related) loci on each arm of chromosome 6. An acceptable donor will match the patient at all or most of the HLA loci.

Conditioning for Hematopoietic Cell Transplantation Conventional Conditioning

The conventional ("classical") practice of allo-HCT involves administration of cytotoxic agents (e.g., cyclophosphamide, busulfan) with or without total body irradiation at doses sufficient to cause bone marrow ablation in the recipient. The beneficial treatment effect of this procedure is due to a combination of the initial eradication of malignant cells and subsequent graft-versus-malignancy effect mediated by non-self-immunologic effector cells. While the slower graft-versus-malignancy effect is considered the potentially curative component, it may be overwhelmed by existing disease in the absence of pretransplant conditioning. Intense conditioning regimens are limited to patients who are sufficiently medically fit to tolerate substantial adverse effects. These include opportunistic infections secondary to loss of endogenous bone marrow function and organ damage or failure caused by cytotoxic drugs.

Subsequent to graft infusion in allo-HCT, immunosuppressant drugs are required to minimize graft rejection and graft-versus-host disease (GVHD), which increases susceptibility to opportunistic infections.

The success of autologous HCT is predicated on the potential of cytotoxic chemotherapy, with or without radiotherapy, to eradicate cancerous cells from the blood and bone marrow. This permits subsequent engraftment and repopulation of the bone marrow with presumably normal hematopoietic stem cells obtained from the patient before undergoing bone marrow ablation. Therefore, autologous HCT is typically performed as consolidation therapy when the patient's disease is in complete remission. Patients who undergo autologous HCT are also susceptible to chemotherapy-related toxicities and opportunistic infections before engraftment, but not GVHD.

Reduced-Intensity Conditioning Allogeneic Hematopoietic Cell Transplantation

Reduced-intensity conditioning (RIC) refers to the pretransplant use of lower doses of cytotoxic drugs or less intense regimens of radiotherapy than are used in traditional full-dose myeloablative conditioning treatments. Although the definition of RIC is variable, with numerous versions employed, all regimens seek to balance the competing effects of relapse due to residual disease and non-relapse mortality. The goal of RIC is to reduce disease burden and to minimize associated treatment-related morbidity and non-relapse mortality in the period during which the beneficial graft-versus-malignancy effect of allogeneic transplantation develops. RIC regimens range from nearly total myeloablative to minimally myeloablative with lymphoablation, with intensity tailored to specific diseases and patient condition. Patients who undergo RIC with allo-HCT initially demonstrate donor cell engraftment and bone marrow mixed chimerism. Most will subsequently convert to full-donor chimerism. In this review, the term reduced-intensity conditioning will refer to all conditioning regimens intended to be nonmyeloablative.

Summary

Description

Hematopoietic cell transplantation (HCT) refers to a procedure by which hematopoietic stem cells are infused to restore bone marrow function in cancer patients who receive bone-marrow-toxic doses of cytotoxic drugs, with or without whole-body radiotherapy. Hematopoietic stem cells may be obtained from the transplant recipient (autologous HCT) or a donor (allogeneic HCT [allo-HCT]). They can be harvested from bone marrow, peripheral blood, or umbilical cord blood shortly after delivery of neonates. Although umbilical cord blood is an allogeneic source, the stem cells in it are antigenically "naive" and thus are associated with a lower incidence of rejection or graft-versus-host disease. Umbilical cord blood is discussed in greater detail in policy #285.

Summary of Evidence

For individuals who have indolent B-cell non-Hodgkin lymphoma (NHL) who receive autologous hematopoietic cell transplant (HCT) as first-line therapy, the evidence includes observational studies, randomized controlled trials (RCTs), and systematic reviews. Relevant outcomes are overall survival (OS), disease-specific survival (DSS), change in disease status, morbid events, and treatment-related mortality and morbidity. The RCTs have not shown a survival advantage with HCT as first-line therapy for indolent B-cell lymphomas; however, RCTs have shown a survival benefit for relapsed disease. Observational studies have shown similar results. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have aggressive B-cell NHL, excluding mantle cell lymphoma (MCL), who receive autologous HCT as consolidation therapy after first complete remission (CR), the evidence includes RCTs and a systematic review. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. While the data from the RCTs offer conflicting results, some data have revealed an OS benefit in patients with aggressive B-cell lymphomas (at high- or high-intermediate risk of relapse) who receive HCT to consolidate a first CR. The RCTs of HCT for relapsed aggressive B-cell lymphomas have also shown an OS benefit with the previously described approach. Results of a retrospective study comparing autologous and allo-HCT for relapsed or refractory B-cell NHL showed more positive outcomes for autologous HCTs. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have NHL, excluding MCL, who receive tandem autologous and allo-HCT, the evidence includes several nonrandomized trials. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. No RCTs have been conducted on the use of tandem HCT for the treatment of NHL, and the published evidence comprises of a limited number of patients. Presently, conclusions on the use of tandem transplants cannot be made about autologous and allo-HCT. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have MCL who receive autologous, allogeneic, or tandem HCT, the evidence includes case series and RCTs. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. Case series and RCTs have shown long-term disease control of this aggressive lymphoma with autologous HCT (with rituximab) to consolidate a first remission; however, the use of autologous HCT in the relapsed setting has not shown improved outcomes. Allo-HCT has shown prolonged disease control in the relapsed or refractory setting. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have peripheral T-cell lymphoma (PTCL) who receive autologous or allo-HCT, the evidence mainly includes prospective trials and case reports/series. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. The role of HCT in PTCL is not well-defined. Few studies have been conducted, and most were performed retrospectively with a limited number of patients; moreover, the patient populations were heterogeneous and included good- and poor-risk patients in the same study. Patient population and characteristics of the studies can be explained partially by the rarity and heterogeneity of the particular group of lymphomas addressed. Additionally, studies of this nature often mix 3 types of patients: 1 type of patient has PTCL not otherwise specified, which has a poorer prognosis; another type has anaplastic lymphoma kinase-positive anaplastic large-cell lymphomas, which has a better prognosis-even with conventional chemotherapy regimens; and a third type has anaplastic lymphoma kinase-negative anaplastic large-cell lymphomas, whifch has a worse prognosis than anaplastic lymphoma kinase-positive anaplastic large-cell lymphomas (but better than patients with PTCL not otherwise specified). For first-line therapy, autologous and allo-HCT were compared in a phase 3 trial, and there were comparable OS and PFS rates between the two groups. Results from recent phase 2 studies with autologous HCT as consolidation offers the best survival outcomes for patients with high-risk features; RCTs to confirm this have not been performed. A single retrospective registry study showed a potential survival benefit among patients treated with allo-HCT in the front-line setting; however, prospective studies are not available. Similarly, high-dose chemothearpy plus consolidation with autologous HCT as the first-line therapy for adults with nodal PTCL demonstrated improved OS and progression-free (PFS) in 2 systematic reviews. Patients with relapsed or refractory PTCL are generally considered incurable with chemotherapy alone. In the salvage setting, data have shown that the use of HCT may improve survival outcomes similar to the results seen in corresponding aggressive B-cell lymphomas in the same treatment setting. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have hepatosplenic T-cell lymphoma (HSTCL) who receive autologous or allo-HCT as consolidation therapy after first response (complete or partial), the evidence includes observational studies and systematic reviews. Relevant outcomes are OS, DSS, change in disease status, morbid events, and treatment-related mortality and morbidity. Two meta-analyses using patient-level data found that consolidation therapy with HCT improves survival in patients with HSTCL. Two small, retrospective studies have shown similar results. A third small, retrospective study showed no significant differences in OS or PFS between allo-HCT and auto-HCT, but the achievement of CR at the time of HCT was associated with improved OS in auto-HCT recipients. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date

Action

2/2025	Appual policy roviow Description summary and references updated Policy
3/2025	Annual policy review. Description, summary, and references updated. Folicy
3/2024	Appual policy review References updated Reliev statements upchanged
0/2024	Policy clarified to include prior authorization requests using Authorization Manager
9/2023	Appuel policy review. Medicelly personanty policy statement added for hepoteonlania
1/2023	Annual policy review. Medically necessary policy statement added for nepatospienic
1/2022	Medicere information removed See MD #122 Medicere Adventage Management for
1/2023	local coverage determination and national coverage determination reference
2/2022	Appual policy review Description summary and references undated Policy
2/2022	statements unchanged.
3/2021	Annual policy review. Description, summary, and references updated. Policy
	statements unchanged.
10/2020	Clarified coding information
4/2020	Bone marrow harvesting codes were removed. Outpatient prior authorization is not
	required.
3/2020	Annual policy review. Description, summary, and references updated. Policy
	statements unchanged.
3/2019	Annual policy review. Description, summary, and references updated. Policy
	statements unchanged.
1/2019	Outpatient prior authorization is required for all commercial products including
	Medicare Advantage. Effective 1/1/2019.
8/2018	Clinical trials for cancer information removed. For information on clinical trials for
	cancer, see subscriber certificate. 8/13/2018
2/2018	Annual policy review. New references added.
2/2018	Clarified coding information.
11/2017	Annual policy review. "Stem" removed from title and policy. HSCT changed to HCT
	in Policy statements otherwise unchanged. 11/1/2017
3/2016	Annual policy review. New references added
3/2015	Annual policy review. New references added
1/2015	Clarified coding information.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective
	10/2015.
4/2013	New references from Annual policy review.
2/2013	Annual policy review. No change in medical policy statement. Effective 2/4/2013.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No
	changes to policy statements.
11/1/2011	Annual policy review. Changes to policy statements.
7/2011	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy
	statements.
7/2009	New policy, effective 7/2009, describing covered and non-covered indications.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use Managed Care Guidelines Indemnity/PPO Guidelines Clinical Exception Process Medical Technology Assessment Guidelines

References

1. National Cancer Institute. Adult Non-Hodgkin Lymphoma Treatment (PDQ)Health Professional Version. 2022; http://www.cancer.gov/cancertopics/pdq/treatment/adult-non-hodgkins/healthprofessional. Accessed December 4, 2024.

- Harris NL, Jaffe ES, Stein H, et al. A revised European-American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. Blood. Sep 01 1994; 84(5): 1361-92. PMID 8068936
- Harris NL, Jaffe ES, Diebold J, et al. The World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues. Report of the Clinical Advisory Committee meeting, Airlie House, Virginia, November, 1997. Ann Oncol. Dec 1999; 10(12): 1419-32. PMID 10643532
- Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. Jul 2022; 36(7): 1720-1748. PMID 35732829
- 5. American Cancer Society. Non-Hodgkin Lymphoma (Adults). https://www.cancer.org/cancer/non-hodgkin-lymphoma/about.html Accessed December 3, 2024.
- 6. Laport GG. The role of hematopoietic cell transplantation for follicular non-Hodgkin's lymphoma. Biol Blood Marrow Transplant. Jan 2006; 12(1 Suppl 1): 59-65. PMID 16399587
- Al Khabori M, de Almeida JR, Guyatt GH, et al. Autologous stem cell transplantation in follicular lymphoma: a systematic review and meta-analysis. J Natl Cancer Inst. Jan 04 2012; 104(1): 18-28. PMID 22190633
- Schaaf M, Reiser M, Borchmann P, et al. High-dose therapy with autologous stem cell transplantation versus chemotherapy or immuno-chemotherapy for follicular lymphoma in adults. Cochrane Database Syst Rev. Jan 18 2012; 1(1): CD007678. PMID 22258971
- Ladetto M, De Marco F, Benedetti F, et al. Prospective, multicenter randomized GITMO/IIL trial comparing intensive (R-HDS) versus conventional (CHOP-R) chemoimmunotherapy in high-risk follicular lymphoma at diagnosis: the superior disease control of R-HDS does not translate into an overall survival advantage. Blood. Apr 15 2008; 111(8): 4004-13. PMID 18239086
- Sebban C, Mounier N, Brousse N, et al. Standard chemotherapy with interferon compared with CHOP followed by high-dose therapy with autologous stem cell transplantation in untreated patients with advanced follicular lymphoma: the GELF-94 randomized study from the Groupe d'Etude des Lymphomes de l'Adulte (GELA). Blood. Oct 15 2006; 108(8): 2540-4. PMID 16835383
- Deconinck E, Foussard C, Milpied N, et al. High-dose therapy followed by autologous purged stemcell transplantation and doxorubicin-based chemotherapy in patients with advanced follicular lymphoma: a randomized multicenter study by GOELAMS. Blood. May 15 2005; 105(10): 3817-23. PMID 15687232
- Lenz G, Dreyling M, Schiegnitz E, et al. Myeloablative radiochemotherapy followed by autologous stem cell transplantation in first remission prolongs progression-free survival in follicular lymphoma: results of a prospective, randomized trial of the German Low-Grade Lymphoma Study Group. Blood. Nov 01 2004; 104(9): 2667-74. PMID 15238420
- Schouten HC, Qian W, Kvaloy S, et al. High-dose therapy improves progression-free survival and survival in relapsed follicular non-Hodgkin's lymphoma: results from the randomized European CUP trial. J Clin Oncol. Nov 01 2003; 21(21): 3918-27. PMID 14517188
- Bozkaya Y, Uncu D, Dağdaş S, et al. Evaluation of Lymphoma Patients Receiving High-Dose Therapy and Autologous Stem Cell Transplantation: Experience of a Single Center. Indian J Hematol Blood Transfus. Sep 2017; 33(3): 361-369. PMID 28824238
- Jiménez-Ubieto A, Grande C, Caballero D, et al. Autologous stem cell transplantation may be curative for patients with follicular lymphoma with early therapy failure who reach complete response after rescue treatment. Hematol Oncol. Dec 2018; 36(5): 765-772. PMID 30129233
- 16. International Non-Hodgkin's Lymphoma Prognostic Factors Project. A predictive model for aggressive non-Hodgkin's lymphoma. N Engl J Med. Sep 30 1993; 329(14): 987-94. PMID 8141877
- 17. Solal-Céligny P, Roy P, Colombat P, et al. Follicular lymphoma international prognostic index. Blood. Sep 01 2004; 104(5): 1258-65. PMID 15126323
- Greb A, Bohlius J, Schiefer D, et al. High-dose chemotherapy with autologous stem cell transplantation in the first line treatment of aggressive non-Hodgkin lymphoma (NHL) in adults. Cochrane Database Syst Rev. Jan 23 2008; 2008(1): CD004024. PMID 18254036
- Haioun C, Lepage E, Gisselbrecht C, et al. Benefit of autologous bone marrow transplantation over sequential chemotherapy in poor-risk aggressive non-Hodgkin's lymphoma: updated results of the prospective study LNH87-2. Groupe d'Etude des Lymphomes de l'Adulte. J Clin Oncol. Mar 1997; 15(3): 1131-7. PMID 9060555

- Kaiser U, Uebelacker I, Abel U, et al. Randomized study to evaluate the use of high-dose therapy as part of primary treatment for "aggressive" lymphoma. J Clin Oncol. Nov 15 2002; 20(22): 4413-9. PMID 12431962
- 21. Kluin-Nelemans HC, Zagonel V, Anastasopoulou A, et al. Standard chemotherapy with or without high-dose chemotherapy for aggressive non-Hodgkin's lymphoma: randomized phase III EORTC study. J Natl Cancer Inst. Jan 03 2001; 93(1): 22-30. PMID 11136838
- 22. Sweetenham JW, Santini G, Qian W, et al. High-dose therapy and autologous stem-cell transplantation versus conventional-dose consolidation/maintenance therapy as postremission therapy for adult patients with lymphoblastic lymphoma: results of a randomized trial of the European Group for Blood and Marrow Transplantation and the United Kingdom Lymphoma Group. J Clin Oncol. Jun 01 2001; 19(11): 2927-36. PMID 11387366
- 23. Fisher RI. Autologous stem-cell transplantation as a component of initial treatment for poor-risk patients with aggressive non-Hodgkin's lymphoma: resolved issues versus remaining opportunity. J Clin Oncol. Nov 15 2002; 20(22): 4411-2. PMID 12431961
- 24. Haioun C, Lepage E, Gisselbrecht C, et al. Survival benefit of high-dose therapy in poor-risk aggressive non-Hodgkin's lymphoma: final analysis of the prospective LNH87-2 protocol--a groupe d'Etude des lymphomes de l'Adulte study. J Clin Oncol. Aug 2000; 18(16): 3025-30. PMID 10944137
- 25. Fisher RI. Autologous bone marrow transplantation for aggressive non-Hodgkin's lymphoma: lessons learned and challenges remaining. J Natl Cancer Inst. Jan 03 2001; 93(1): 4-5. PMID 11136829
- Hahn T, Wolff SN, Czuczman M, et al. The role of cytotoxic therapy with hematopoietic stem cell transplantation in the therapy of diffuse large cell B-cell non-Hodgkin's lymphoma: an evidence-based review. Biol Blood Marrow Transplant. 2001; 7(6): 308-31. PMID 11464975
- 27. Kimby E, Brandt L, Nygren P, et al. A systematic overview of chemotherapy effects in aggressive non-Hodgkin's lymphoma. Acta Oncol. 2001; 40(2-3): 198-212. PMID 11441932
- Philip T, Biron P. High-dose chemotherapy and autologous bone marrow transplantation in diffuse intermediate- and high-grade non-Hodgkin lymphoma. Crit Rev Oncol Hematol. Feb 2002; 41(2): 213-23. PMID 11856597
- 29. Betticher DC, Martinelli G, Radford JA, et al. Sequential high dose chemotherapy as initial treatment for aggressive sub-types of non-Hodgkin lymphoma: results of the international randomized phase III trial (MISTRAL). Ann Oncol. Oct 2006; 17(10): 1546-52. PMID 16888080
- Baldissera RC, Nucci M, Vigorito AC, et al. Frontline therapy with early intensification and autologous stem cell transplantation versus conventional chemotherapy in unselected high-risk, aggressive non-Hodgkin's lymphoma patients: a prospective randomized GEMOH report. Acta Haematol. 2006; 115(1-2): 15-21. PMID 16424644
- Olivieri A, Santini G, Patti C, et al. Upfront high-dose sequential therapy (HDS) versus VACOP-B with or without HDS in aggressive non-Hodgkin's lymphoma: long-term results by the NHLCSG. Ann Oncol. Dec 2005; 16(12): 1941-8. PMID 16157621
- 32. Stiff PJ, Unger JM, Cook JR, et al. Autologous transplantation as consolidation for aggressive non-Hodgkin's lymphoma. N Engl J Med. Oct 31 2013; 369(18): 1681-90. PMID 24171516
- Casasnovas RO, Ysebaert L, Thieblemont C, et al. FDG-PET-driven consolidation strategy in diffuse large B-cell lymphoma: final results of a randomized phase 2 study. Blood. Sep 14 2017; 130(11): 1315-1326. PMID 28701367
- Strüßmann T, Fritsch K, Baumgarten A, et al. Favourable outcomes of poor prognosis diffuse large Bcell lymphoma patients treated with dose-dense Rituximab, high-dose Methotrexate and six cycles of CHOP-14 compared to first-line autologous transplantation. Br J Haematol. Sep 2017; 178(6): 927-935. PMID 28643323
- Qualls D, Sullivan A, Li S, et al. High-dose Thiotepa, Busulfan, Cyclophosphamide, and Autologous Stem Cell Transplantation as Upfront Consolidation for Systemic Non-Hodgkin Lymphoma With Synchronous Central Nervous System Involvement. Clin Lymphoma Myeloma Leuk. Dec 2017; 17(12): 884-888. PMID 28870642
- Jaffe ES. The 2008 WHO classification of lymphomas: implications for clinical practice and translational research. Hematology Am Soc Hematol Educ Program. 2009: 523-31. PMID 20008237
- Philip T, Guglielmi C, Hagenbeek A, et al. Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma. N Engl J Med. Dec 07 1995; 333(23): 1540-5. PMID 7477169

- Fujita N, Kobayashi R, Atsuta Y, et al. Hematopoietic stem cell transplantation in children and adolescents with relapsed or refractory B-cell non-Hodgkin lymphoma. Int J Hematol. Apr 2019; 109(4): 483-490. PMID 30701466
- Monjanel H, Deconinck E, Perrodeau E, et al. Long-term follow-up of tandem high-dose therapy with autologous stem cell support for adults with high-risk age-adjusted international prognostic index aggressive non-Hodgkin Lymphomas: a GOELAMS pilot study. Biol Blood Marrow Transplant. Jun 2011; 17(6): 935-40. PMID 21109011
- 40. Papadopoulos KP, Noguera-Irizarry W, Wiebe L, et al. Pilot study of tandem high-dose chemotherapy and autologous stem cell transplantation with a novel combination of regimens in patients with poor risk lymphoma. Bone Marrow Transplant. Sep 2005; 36(6): 491-7. PMID 16044139
- 41. Tarella C, Zanni M, Di Nicola M, et al. Prolonged survival in poor-risk diffuse large B-cell lymphoma following front-line treatment with rituximab-supplemented, early-intensified chemotherapy with multiple autologous hematopoietic stem cell support: a multicenter study by GITIL (Gruppo Italiano Terapie Innovative nei Linfomi). Leukemia. Aug 2007; 21(8): 1802-11. PMID 17554382
- 42. Satwani P, Jin Z, Martin PL, et al. Sequential myeloablative autologous stem cell transplantation and reduced intensity allogeneic hematopoietic cell transplantation is safe and feasible in children, adolescents and young adults with poor-risk refractory or recurrent Hodgkin and non-Hodgkin lymphoma. Leukemia. Feb 2015; 29(2): 448-55. PMID 24938649
- 43. Banks PM, Chan J, Cleary ML, et al. Mantle cell lymphoma. A proposal for unification of morphologic, immunologic, and molecular data. Am J Surg Pathol. Jul 1992; 16(7): 637-40. PMID 1530105
- 44. Hoster E, Dreyling M, Klapper W, et al. A new prognostic index (MIPI) for patients with advancedstage mantle cell lymphoma. Blood. Jan 15 2008; 111(2): 558-65. PMID 17962512
- 45. Dreyling M, Lenz G, Hoster E, et al. Early consolidation by myeloablative radiochemotherapy followed by autologous stem cell transplantation in first remission significantly prolongs progression-free survival in mantle-cell lymphoma: results of a prospective randomized trial of the European MCL Network. Blood. Apr 01 2005; 105(7): 2677-84. PMID 15591112
- 46. Dreyling M, Doorduijn J, Giné E, et al. Ibrutinib combined with immunochemotherapy with or without autologous stem-cell transplantation versus immunochemotherapy and autologous stem-cell transplantation in previously untreated patients with mantle cell lymphoma (TRIANGLE): a three-arm, randomised, open-label, phase 3 superiority trial of the European Mantle Cell Lymphoma Network. Lancet. May 25 2024; 403(10441): 2293-2306. PMID 38705160
- 47. Zoellner AK, Unterhalt M, Stilgenbauer S, et al. Long-term survival of patients with mantle cell lymphoma after autologous haematopoietic stem-cell transplantation in first remission: a post-hoc analysis of an open-label, multicentre, randomised, phase 3 trial. Lancet Haematol. Sep 2021; 8(9): e648-e657. PMID 34450102
- Till BG, Gooley TA, Crawford N, et al. Effect of remission status and induction chemotherapy regimen on outcome of autologous stem cell transplantation for mantle cell lymphoma. Leuk Lymphoma. Jun 2008; 49(6): 1062-73. PMID 18452065
- 49. García-Noblejas A, Cannata-Ortiz J, Conde E, et al. Autologous stem cell transplantation (ASCT) in patients with mantle cell lymphoma: a retrospective study of the Spanish lymphoma group (GELTAMO). Ann Hematol. Aug 2017; 96(8): 1323-1330. PMID 28536895
- Metzner B, Müller TH, Casper J, et al. Long-term outcome in patients with mantle cell lymphoma following high-dose therapy and autologous stem cell transplantation. Eur J Haematol. Aug 2023; 111(2): 220-228. PMID 37094812
- 51. Villanueva ML, Vose JM. The role of hematopoietic stem cell transplantation in non-Hodgkin lymphoma. Clin Adv Hematol Oncol. Jul 2006; 4(7): 521-30. PMID 17147239
- Khouri IF, Lee MS, Saliba RM, et al. Nonablative allogeneic stem-cell transplantation for advanced/recurrent mantle-cell lymphoma. J Clin Oncol. Dec 01 2003; 21(23): 4407-12. PMID 14645431
- Maris MB, Sandmaier BM, Storer BE, et al. Allogeneic hematopoietic cell transplantation after fludarabine and 2 Gy total body irradiation for relapsed and refractory mantle cell lymphoma. Blood. Dec 01 2004; 104(12): 3535-42. PMID 15304387
- 54. Krüger WH, Hirt C, Basara N, et al. Allogeneic stem cell transplantation for mantle cell lymphomaupdate of the prospective trials of the East German Study Group Hematology/Oncology (OSHO#60 and #74). Ann Hematol. Jun 2021; 100(6): 1569-1577. PMID 33829299

- Tam CS, Bassett R, Ledesma C, et al. Mature results of the M. D. Anderson Cancer Center riskadapted transplantation strategy in mantle cell lymphoma. Blood. Apr 30 2009; 113(18): 4144-52. PMID 19168784
- 56. Geisler C. Mantle cell lymphoma: are current therapies changing the course of disease?. Curr Oncol Rep. Sep 2009; 11(5): 371-7. PMID 19679012
- 57. Zhai Y, Wang J, Jiang Y, et al. The efficiency of autologous stem cell transplantation as the first-line treatment for nodal peripheral T-cell lymphoma: results of a systematic review and meta-analysis. Expert Rev Hematol. Mar 2022; 15(3): 265-272. PMID 35152814
- 58. Girard L, Koh YJ, Koh LP, et al. Role of upfront autologous transplant for peripheral T-cell lymphoma patients achieving a complete remission with first-line therapy: a systematic review and meta-analysis. Bone Marrow Transplant. Jun 2024; 59(6): 838-848. PMID 38443704
- 59. Schmitz N, Truemper L, Bouabdallah K, et al. A randomized phase 3 trial of autologous vs allogeneic transplantation as part of first-line therapy in poor-risk peripheral T-NHL. Blood. May 13 2021; 137(19): 2646-2656. PMID 33512419
- 60. Reimer P. Impact of autologous and allogeneic stem cell transplantation in peripheral T-cell lymphomas. Adv Hematol. 2010; 2010: 320624. PMID 21253465
- 61. Corradini P, Tarella C, Zallio F, et al. Long-term follow-up of patients with peripheral T-cell lymphomas treated up-front with high-dose chemotherapy followed by autologous stem cell transplantation. Leukemia. Sep 2006; 20(9): 1533-8. PMID 16871285
- 62. Mercadal S, Briones J, Xicoy B, et al. Intensive chemotherapy (high-dose CHOP/ESHAP regimen) followed by autologous stem-cell transplantation in previously untreated patients with peripheral T-cell lymphoma. Ann Oncol. May 2008; 19(5): 958-63. PMID 18303032
- 63. Rodríguez J, Conde E, Gutiérrez A, et al. Frontline autologous stem cell transplantation in high-risk peripheral T-cell lymphoma: a prospective study from The Gel-Tamo Study Group. Eur J Haematol. Jul 2007; 79(1): 32-8. PMID 17598836
- 64. Wang J, Wei L, Ye J, et al. Autologous hematopoietic stem cell transplantation may improve longterm outcomes in patients with newly diagnosed extranodal natural killer/T-cell lymphoma, nasal type: a retrospective controlled study in a single center. Int J Hematol. Jan 2018; 107(1): 98-104. PMID 28856590
- 65. Wu M, Wang F, Zhao S, et al. Autologous hematopoietic stem cell transplantation improves survival outcomes in peripheral T-cell lymphomas: a multicenter retrospective real-world study. Ann Hematol. Nov 2023; 102(11): 3185-3193. PMID 37700194
- 66. Mamez AC, Dupont A, Blaise D, et al. Allogeneic stem cell transplantation for peripheral T cell lymphomas: a retrospective study in 285 patients from the Société Francophone de Greffe de Moelle et de Thérapie Cellulaire (SFGM-TC). J Hematol Oncol. May 19 2020; 13(1): 56. PMID 32429979
- Du J, Yu D, Han X, et al. Comparison of Allogeneic Stem Cell Transplant and Autologous Stem Cell Transplant in Refractory or Relapsed Peripheral T-Cell Lymphoma: A Systematic Review and Metaanalysis. JAMA Netw Open. May 03 2021; 4(5): e219807. PMID 34042995
- Song KW, Mollee P, Keating A, et al. Autologous stem cell transplant for relapsed and refractory peripheral T-cell lymphoma: variable outcome according to pathological subtype. Br J Haematol. Mar 2003; 120(6): 978-85. PMID 12648067
- 69. Rodríguez J, Conde E, Gutiérrez A, et al. The adjusted International Prognostic Index and beta-2microglobulin predict the outcome after autologous stem cell transplantation in relapsing/refractory peripheral T-cell lymphoma. Haematologica. Aug 2007; 92(8): 1067-74. PMID 17640855
- 70. Kyriakou C, Canals C, Finke J, et al. Allogeneic stem cell transplantation is able to induce long-term remissions in angioimmunoblastic T-cell lymphoma: a retrospective study from the lymphoma working party of the European group for blood and marrow transplantation. J Clin Oncol. Aug 20 2009; 27(24): 3951-8. PMID 19620487
- Klebaner D, Koura D, Tzachanis D, et al. Intensive Induction Therapy Compared With CHOP for Hepatosplenic T-cell Lymphoma. Clin Lymphoma Myeloma Leuk. Jul 2020; 20(7): 431-437.e2. PMID 32284297
- 72. Rashidi A, Cashen AF. Outcomes of allogeneic stem cell transplantation in hepatosplenic T-cell lymphoma. Blood Cancer J. Jun 05 2015; 5(6): e318. PMID 26047388
- 73. Voss MH, Lunning MA, Maragulia JC, et al. Intensive induction chemotherapy followed by early highdose therapy and hematopoietic stem cell transplantation results in improved outcome for patients

with hepatosplenic T-cell lymphoma: a single institution experience. Clin Lymphoma Myeloma Leuk. Feb 2013; 13(1): 8-14. PMID 23107915

- 74. Tanase A, Schmitz N, Stein H, et al. Allogeneic and autologous stem cell transplantation for hepatosplenic T-cell lymphoma: a retrospective study of the EBMT Lymphoma Working Party. Leukemia. Mar 2015; 29(3): 686-8. PMID 25234166
- Moustafa MA, Ramdial JL, Tsalatsanis A, et al. A US Multicenter Collaborative Study on Outcomes of Hematopoietic Cell Transplantation in Hepatosplenic T-Cell Lymphoma. Transplant Cell Ther. May 2024; 30(5): 516.e1-516.e10. PMID 38431075
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas. Version 3.2024. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed December 3, 2024.
- 77. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: T-Cell Lymphomas. Version 1.2025. https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed December 4, 2024.
- Munshi PN, Hamadani M, Kumar A, et al. ASTCT, CIBMTR, and EBMT clinical practice recommendations for transplant and cellular therapies in mantle cell lymphoma. Bone Marrow Transplant. Dec 2021; 56(12): 2911-2921. PMID 34413469
- 79. Epperla N, Kumar A, Abutalib SA, et al. ASTCT Clinical Practice Recommendations for Transplantation and Cellular Therapies in Diffuse Large B Cell Lymphoma. Transplant Cell Ther. Sep 2023; 29(9): 548-555. PMID 37419325
- 80. Iqbal M, Kumar A, Dreger P, et al. Clinical Practice Recommendations for Hematopoietic Cell Transplantation and Cellular Therapies in Follicular Lymphoma: A Collaborative Effort on Behalf of the American Society for Transplantation and Cellular Therapy and the European Society for Blood and Marrow Transplantation. Transplant Cell Ther. Sep 2024; 30(9): 832-843. PMID 38972511
- Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Stem Cell Transplantation (Formerly 110.8.1) (110.23). 2016; https://www.cms.gov/medicare-coveragedatabase/details/ncd-

details.aspx?NCDId=366&ncdver=1&DocID=110.23&list_type=ncd&bc=gAAAAAgAAAAAAA%3d%3d &. Accessed December 3, 2024.