



Autologous and allogeneic haematopoietic cell transplantation in adult patients with Hodgkin lymphoma: recommendations from the EBMT Practice Harmonisation and Guidelines Committee and Lymphoma Working Party

Ali Bazarbachi, Ranjana Advani, Sairah Ahmed, Carmelo Carlo-Stella, Luca Castagna, Dennis A Eichenauer, Jean El-Cheikh, Mehdi Hamadani, Carmen Martinez, Emma Nicholson, Karl S Peggs, Miguel-Angel Perales, Norbert Schmitz, Lena Specht, Alina Daniela Tanase, Francesco Onida, Annalisa Ruggeri, Cédric Rossi, Mahmoud Aljurf, Marc André, Isabel Sánchez-Ortega, Ibrahim Yakoub-Agha, Anna Sureda

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Bone Marrow Transplantation Program, Department of Internal Medicine, American University of Beirut, Beirut, Lebanon (Prof A Bazarbachi MD, J El-Cheikh MD); Stanford University School of Medicine, Division of Oncology, Stanford, CA, USA (Prof R Advani MD); MD Anderson Cancer Center, Departments of Lymphoma, Myeloma and Stem Cell Transplant, and Cellular Therapy, Houston, TX, USA (Prof S Ahmed MD); Department of Biomedical Sciences, Humanitas University, Milano, Italy (Prof C Carlo-Stella MD); Department of Oncology and Hematology IRCCS Humanitas Research Hospital, Milano, Italy (Prof C Carlo-Stella); Bone Marrow Transplant Unit, Azienda Ospedaliera Riunita Villa Sofia Cervello, Palermo, Italy (L Castagna MD); University of Cologne, First Department of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Dusseldorf, German Hodgkin Study Group, Cologne, Germany (D A Eichenauer MD); Medical College of Wisconsin and Center for International Blood and Marrow Transplant Research, Division of Hematology and Oncology, Milwaukee, WI, USA (Prof M Hamadani MD); Hematology Department, Institute of Cancer and Hematological Diseases, Hospital Clínic de Barcelona, Barcelona, Spain (C Martinez MD); August Pi i Sunyer Biomedical Research Institute, Barcelona, Spain (C Martinez); University of Barcelona, Barcelona, Spain (C Martinez); Department of Haematology, The Royal Marsden NHS Foundation

The European Group for Blood and Bone Marrow transplantation Practice Harmonization and Guidelines Committee together with the Lymphoma Working Party convened 23 experts in Hodgkin lymphoma, transplantation, and radiation oncology, to develop consensus recommendations on the use of autologous and allogeneic haematopoietic cell transplantation (HCT) in relapsed or refractory Hodgkin lymphoma. Through a structured literature review and a 2-day workshop in Berlin, Germany, on Sept 29 and 30, 2025, the panel established guidance across major clinical decision points. The outcome of this review and workshop include the following recommendations. Salvage therapy should include brentuximab vedotin or checkpoint inhibitors, or both, with metabolic complete response preferred before autologous HCT. BEAM (carmustine, etoposide, cytarabine and melphalan) remains the most commonly used conditioning regimen, and autologous HCT continues to be the standard for chemosensitive relapse. Peri-transplantation radiotherapy could be considered for PET-positive or residual disease. Brentuximab vedotin consolidation is recommended for patients at high-risk. Allogeneic HCT is advised for eligible patients who relapse after autologous HCT, ideally with reduced intensity conditioning and post-transplantation cyclophosphamide as graft-versus-host disease prophylaxis. Routine maintenance after allogeneic HCT is not recommended; relapse management should be tailored and can involve donor lymphocyte infusion, brentuximab vedotin, checkpoint inhibitors, chemotherapy, radiotherapy, or clinical trial enrolment.

Introduction

Classical Hodgkin lymphoma is a highly curable disease with over 70% of patients with advanced disease and over 90% of patients with early-stage disease reaching cure with multiagent chemotherapy with or without radiotherapy in the pre-novel agent era.¹ Given that classical Hodgkin lymphoma accounts for approximately 90–95% of Hodgkin lymphoma cases, from herein we will refer to it simply as Hodgkin lymphoma. For primary refractory or relapsed patients, the standard of care is salvage chemotherapy followed by autologous haematopoietic cell transplantation (HCT).² Best outcomes are seen in patients who reach a complete response to salvage therapy before autologous HCT, yet less than 50% of patients reached complete response with chemotherapy-based salvage. Allogeneic HCT represents a curative strategy for patients who do not respond to autologous HCT.² The introduction of novel agents, namely brentuximab vedotin and checkpoint inhibitors, such as nivolumab and pembrolizumab, has changed the landscape of Hodgkin lymphoma treatment in the last decade, both in the frontline^{3–6} and relapsed or refractory settings.^{7–25} Incorporation of brentuximab vedotin or checkpoint inhibitors, or both, in salvage regimens before autologous HCT,^{7–14} consolidation after autologous HCT for patients at high-risk,^{12,13,15} salvage for relapse after autologous HCT,^{16–18} bridge to allogeneic HCT,^{19–22} and relapse after allogeneic HCT^{23–25} resulted in improved post-transplantation outcomes over time.

Overall, the number of transplantations being performed are declining because of increasing cure rates in the frontline and first relapse setting.

Given the rapidly evolving treatment landscape for both newly diagnosed and relapsed or refractory Hodgkin lymphoma, consensus is lacking regarding the best treatment approach and sequencing of novel agents, including indication and timing for autologous and allogeneic HCT. Therefore, the European Society for Blood and Marrow Transplantation (EBMT) Practice and Harmonization and Guidelines Committee and the Lymphoma Working Party (LWP) of the EBMT set out to develop best practice recommendations for managing adult patients with Hodgkin lymphoma undergoing autologous HCT or allogeneic HCT.

Methods

This workshop was conducted according to the methodology published by the EBMT Practice Harmonization and Guidelines Committee.²⁶ On March 4, 2025, the LWP of the EBMT appointed two project leaders (AB and AS) with the objective to establish consensus-based recommendations on autologous HCT and allogeneic HCT in the management of relapsed or refractory Hodgkin lymphoma. To achieve this aim, a panel of 16 international experts (AB, RA, SA, CC-S, LC, DAE, JE-C, MH, CM, EN, KSP, M-AP, NS, LS, ADT, and AS) from seven countries (Italy, Germany, Spain, the UK, Denmark, Lebanon, and the USA),

recognised for their expertise in Hodgkin lymphoma and HCT, was convened under the guidance of the EBMT, the LWP of EBMT, and the EBMT Practice Harmonization and Guidelines Committee. Expert selection was conducted by the leaders of this project (AB is the LWP chair and AS is a co-leader of the Hodgkin lymphoma subcommittee) based on their professional expertise and willingness to contribute actively to the initiative. All selected experts are listed as co-authors. Key methodological aspects and project topics were discussed between the selected experts, and the EBMT Practice Harmonization and Guidelines Committee. Experts were organised into subgroups, each focusing on specific themes. The final list of key questions and topics was collectively agreed upon by all participating experts. A total of seven subgroups were convened: four focusing on autologous HCT and three on allogenic HCT. The autologous HCT subgroups addressed: optimal salvage regimen before autologous HCT and the role of metabolic complete response before autologous HCT, patient selection and optimal conditioning regimens, the role of radiotherapy before or after autologous HCT, and consolidation and maintenance strategies (including choice of agents, duration, and the effect of pre-transplantation exposure and sensitivity). The allogenic HCT subgroups addressed: indications and sequencing treatments before allogenic HCT, transplantation procedures (including donor selection, conditioning regimens, and graft-versus-host disease [GVHD] prophylaxis), and post-transplantation management (including maintenance strategies and treatment of relapse after allogenic HCT). A 2-day workshop was held in Berlin, Germany, on Sept 29 and 30, 2025, bringing together ten experts (AB, AS, DAE, JE-C, CM, EN, KSP, M-AP, NS, and ADT) on-site, and six others (RA, SA, CC-S, LC, MH, and LS) participated during the pre-meeting preparation phase. Each thematic area was presented by subgroups of two or four experts who compiled literature findings, followed by open discussions that aimed at refining recommendations.

In line with the recommendations of the EBMT Practice Harmonization and Guidelines Committee, the first draft of this Review was circulated to external experts for comprehensive review and broader consensus. These experts (FO, AR, CR, MAI, MAn, and IY-A) were therefore included as authors. Given the scarcity of randomised trial data and the inadequate evidence base for many clinical scenarios, recommendations were not formally graded. Instead, a structured consensus approach was used incorporating iterative expert discussions. Once the initial recommendations were formulated, multiple rounds of discussion with all 23 authors were done to ensure validation. We have divided this Review into two parts (autologous HCT and allogenic HCT) and attempted to answer each question by first presenting the current state of the art treatment, followed by the panel's recommendation for each question. The final

recommendations underwent a final review and approval by all expert participants. The EBMT provided logistical support for the meeting.

EBMT recommendations

Table 1 shows the EBMT recommendations with comments for each question and issue related to autologous HCT and table 2 shows the recommendations with comments for each question and issue related to allogenic HCT.

Autologous HCT

Which patients with Hodgkin lymphoma are candidates for autologous HCT?

Autologous HCT remains the standard approach for primary refractory or relapsed Hodgkin lymphoma with chemosensitive disease.² Two studies (performed before PET-CT scan-adapted strategies and before the advent of checkpoint inhibitors and brentuximab vedotin) showed long-term remission in 50% of patients treated with salvage chemotherapy and autologous HCT.^{27,28} For patients treated with salvage chemotherapy regimens, primary refractory disease, or early relapse within 12 months post-first-line therapy are adverse prognostic factors for post-autologous HCT, with a 3-year freedom from treatment failure (FFTF) of 41% and overall survival of 43% for those with primary refractory or early relapses compared with a FFTF of 75% and overall survival of 93% for those with late relapses.²⁸ In patients treated with salvage chemotherapy, failure to reach a PET-CT negative response before autologous HCT is the most powerful predictor of outcome although the number of cycles required to reach metabolic complete response does not affect long-term survival. Additional salvage to reach metabolic complete response is better than proceeding to autologous HCT in partial response.²⁹ Phase 2 studies of checkpoint inhibitor-based or brentuximab vedotin-based salvage showed impressive and, to date, durable progression-free survival rates exceeding 90% for those proceeding to autologous HCT in complete response, although follow up remains short.^{12–14,30}

A subset of patients who relapsed (especially after initial treatment for early-stage favourable disease) reach durable disease control without the use of high-dose therapy and autologous HCT.³¹ In paediatric and young adult patients, a phase 2 study in low-risk relapsed or refractory Hodgkin lymphoma used brentuximab vedotin–nivolumab followed by involved site consolidation using PET-adapted strategy and showed excellent progression-free survival at 3 years.³² In adults, a phase 2b randomised controlled trial of brentuximab vedotin–etoposide plus solumedrol plus high-dose cytarabine plus cisplatin (ESHAP) versus ESHAP followed by brentuximab vedotin consolidation is assessing the role of brentuximab vedotin consolidation without autologous HCT for those with metabolic complete response. Median follow up for the trial is short

Trust, London, UK (E Nicholson MD); University College London Hospitals NHS Foundation Trust, London, UK (Prof K S Peggs MD); Memorial Sloan Kettering Cancer Center, Adult Bone Marrow Transplant Service, Department of Medicine, New York, NY, USA (Prof M-A Perales MD); Department of Medicine A, Hematology and Oncology, University Hospital of Muenster, Muenster, Germany (Prof N Schmitz MD); Department of Oncology, Copenhagen University Hospital-Rigshospitalet, Copenhagen, Denmark (Prof L Specht MD); Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark (Prof L Specht); Carol Davila University of Medicine and Pharmacy, Fundeni Clinical Institute, Bucharest, Romania (A D Tanase MD); the European Group for Blood and Bone Marrow transplantation Practice Harmonisation and Guidelines Committee, Hematology and Bone Marrow Transplant Centre, ASST Fatebenefratelli-Sacco, University of Milan, Milan, Italy (Prof F Onida MD); the European Group for Blood and Bone Marrow transplantation Practice Harmonisation and Guidelines Committee, IRCCS Ospedale San Raffaele, Hematology and Bone Marrow Transplantation Unit, Milan, Italy (A Ruggeri MD); Université Bourgogne Europe, CHU Dijon Bourgogne, Hématologie, INSERM1231 CTM Equipe Epi2THM, Dijon, France (Prof C Rossi MD); King Faisal Specialist Hospital and Research Centre, Department of Oncology, Riyadh, Saudi Arabia (M Aljurj MD); Centre Hospitalier Universitaire UCL Namur, Department of Hematology, Université Catholique de Louvain, Yvoir, Belgium (Prof M André MD); the European Group for Blood and Bone Marrow transplantation Practice Harmonisation and Guidelines Committee, the European Group for Blood and Bone Marrow transplantation Chief Medical Officer, Executive Office, Barcelona, Spain (I Sanchez-Ortega MD);

	EBMT recommendation	Comment
Which patients are candidates for autologous HCT?	Refractory or relapsed patients in advanced stage and sensitive disease after salvage therapy	For patients with early-stage disease and abbreviated previous therapy, treatment with chemotherapy with or without brentuximab vedotin or checkpoint inhibitors with or without radiotherapy can be considered
What is the optimal salvage therapy regimen before autologous HCT?	Brentuximab vedotin or checkpoint inhibitors to be included in salvage therapy	The decision between brentuximab vedotin, checkpoint inhibitors or both will depend on: previous treatments received, disease stage and tumour bulk at relapse, and time to relapse
Is reaching a mCR essential before proceeding with autologous HCT?	mCR should be attempted to be reached before autologous HCT using salvage chemotherapy with or without new drugs (including brentuximab vedotin and checkpoint inhibitors)	Autologous HCT is recommended in patients with partial response with low-volume disease if they received brentuximab vedotin and checkpoint inhibitors as part of salvage regimen
What is the role of radiotherapy before or after autologous HCT?	When considered, early consultation with a radiation oncologist is recommended; radiotherapy to PET-positive lesions before autologous HCT could be considered; radiotherapy can be considered for patients with persistent PET-positive lesions after autologous HCT	Radiotherapy including a clinically significant dose to the lungs should be used cautiously
What is the optimal conditioning regimen before autologous HCT?	No prospective randomised trials indicate the superiority of any preparatory regimen; however, BEAM is the most frequently used conditioning regimen	In case of shortage of BCNU, LEAM or thiotepa (5–7 mg/kg maximum) are an option
Which patients should receive consolidation after autologous HCT?	Brentuximab vedotin consolidation in brentuximab vedotin-naïve patients with classical Hodgkin lymphoma without complete remission pre-transplantation and/or with one or more high risk factor (following the AETHERA trial); off-label checkpoint inhibitor consolidation (eg, pembrolizumab and nivolumab) can be considered in patients with classical Hodgkin lymphoma with high-risk factors and brentuximab vedotin-refractory disease or brentuximab vedotin-intolerance; off-label consolidation with brentuximab vedotin and checkpoint inhibitors can be considered in patients who are not refractory and not intolerant to brentuximab vedotin	Brentuximab vedotin consolidation in patients with classical Hodgkin lymphoma with one or more high risk factor and minimal previous brentuximab vedotin exposure (1–6 cycles), provided no brentuximab vedotin-refractoriness and no previous neurotoxicity; the benefit of checkpoint inhibitors should be weighed against potential immune-related side-effects; radiotherapy can be considered for patients with persistent PET-positive lesions after autologous HCT
Duration of the post-transplantation consolidation or maintenance therapy	Recommended brentuximab vedotin duration: up to 16 cycles total (including pre-autologous HCT), unless unacceptable toxicity or relapse or progression	NA

mCR=metabolic complete remission. BEAM=carmustine, etoposide, cytarabine, and melphalan. BCNU=carmustine. LEAM=lomustine, etoposide, cytarabine, and melphalan. NA=not applicable.

Table 1: EBMT recommendation on autologous HCT in patients with Hodgkin lymphoma

	EBMT recommendation	Comment
Which patients with Hodgkin lymphoma are candidates for allogeneic HCT?	Consolidation with allogeneic HCT is recommended for eligible patients, post-brentuximab vedotin and post-checkpoint inhibitor exposure (eligibility defined as relapse after autologous HCT, adequate organ function and physical condition, and sensitive disease before allogeneic HCT); for refractory patients, decision to allograft should be done on an individual basis; time interval between the last dose of checkpoint inhibitors and allogeneic HCT is preferably at least 6 weeks if clinically feasible; consider the use of bridging therapy before allogeneic HCT to reduce the risk of relapse	Allogeneic HCT can be postponed in patients with complete remission post-checkpoint inhibitors as many of these patients can reach long-lasting remission and some of them are possibly cured
Transplantation modalities		
Donor selection	In order of preference: HLA-matched sibling donor, HLA-matched unrelated donor, and HLA-haplo identical donor or HLA-mismatched unrelated donor	Cord blood should be avoided in adults except if no alternative donor is available
Conditioning regimen	Reduced intensity conditioning (such as Flu-Mel, FB2, or FC-TBI) are preferred; in patients with high relapse risk, conditioning regimens with higher intensity (but reduced organ toxicity) may be considered (eg, T1B2F); BEAM-based conditioning could be considered in allogeneic HCT as a first transplant	NA
GVHD prophylaxis	PTCy is the recommended GVHD prophylaxis independently of the donor (particularly in checkpoint inhibitor pre-treated patients)	Other methods of T cell depletion, such as antithymocyte globulin or alemtuzumab plus DLI, could be considered for HLA-identical siblings or unrelated donor
How to prevent and manage relapse after allogeneic HCT?	There is no recommendation for maintenance therapy after allogeneic HCT outside of clinical trials; clinical trials and new biomarkers should be developed to make a recommendation on maintenance therapy; treatment of relapse should include the following: rapid tapering of immunosuppression, DLI with or without brentuximab vedotin (checkpoint inhibitors should be used with caution), chemotherapy, brentuximab vedotin, checkpoint inhibitors with caution, and radiotherapy, as well as more prospective clinical trials including trials on cellular therapy	Radiotherapy can be considered for patients with persistent PET-positive lesions after allogeneic HCT

BEAM=carmustine, etoposide, cytarabine, and melphalan. BCNU=carmustine. DLI=donor lymphocyte infusion. Flu-Mel=fludarabine and melphalan. FB2=fludarabine and busulfan. FC-TBI=fludarabine, cyclophosphamide, total body irradiation. T1B2F=thiotepa, busulfan, and fludarabine. GVHD=graft-versus-host disease. NA=not applicable. PTCy=post-transplant cyclophosphamide.

Table 2: EBMT recommendation on allogeneic HCT in patients with Hodgkin lymphoma

at 10 months but an estimated progression-free survival of 74% at 24 months was shown.³³ The predictive value of PET-CT in patients who have had previous checkpoint inhibitor therapy is less well defined, and the effect of previous exposure to brentuximab vedotin with or without checkpoint inhibitors in the first-line setting and how this could affect second-line management is still not clear. Finally, outcomes after pembrolizumab–gemcitabine, vinorelbine and liposomal doxorubicin without transplantation were inferior to those of the pembrolizumab–gemcitabine, vinorelbine and liposomal doxorubicin with autologous HCT.³⁴ In summary, despite high rates of response, long-term disease control with transplantation-free strategies after checkpoint inhibitor-based salvage remains unproven outside selected low-risk populations, hence autologous HCT remains recommended as standard of care.

The workshop recommendations were that autologous HCT is the standard of care for relapsed or refractory patients in advanced stage and sensitive disease after salvage therapy and that for patients who relapsed with early-stage disease and abbreviated previous therapy, treatment with chemotherapy with or without brentuximab vedotin or checkpoint inhibitors, or both, with or without radiotherapy can be considered.

What is the optimal salvage therapy regimen before autologous HCT in patients with Hodgkin lymphoma?

Multiple chemotherapy regimens have been used in the past as salvage before autologous HCT,^{29,35–39} with no proven superiority of any of them. In the past decade, incorporation of brentuximab vedotin or checkpoint inhibitors into these regimens^{7–14} substantially improved response rates, resulting in metabolic complete response in more than 70% of patients.^{7–14} As such, these chemoimmunotherapy combinations have largely replaced chemotherapy alone for relapsed or refractory Hodgkin lymphoma before autologous HCT.

The workshop recommendations were to include brentuximab vedotin or checkpoint inhibitors, or both, to salvage chemotherapy; the decision will depend on previous treatments received, disease stage, and tumour bulk at relapse and the time to relapse.

Is reaching metabolic complete response essential before proceeding with autologous HCT?

Although data show that reaching metabolic complete response before autologous HCT is highly predictive for durable response post-transplantation,^{40,41} it is not the only factor predicting post-autologous HCT outcomes. It is reasonable to proceed to autologous HCT with a good partial response with minimal tumour volume if checkpoint inhibitor-based and brentuximab vedotin-based salvage therapy (either monotherapy or in combination) has been exhausted as there continues to be a benefit for patients with autologous HCT. Importantly, PET-CT positivity post-checkpoint inhibitors can reflect

immune-related inflammation. Clinical judgment and disease kinetics should complement PET-CT in the decision making. Moreover, several retrospective studies in patients with primary refractory or early relapsed Hodgkin lymphoma have shown that chemotherapy administered after checkpoint inhibitor exposure can be effective in inducing complete response, likely reflecting chemotherapy re-sensitisation.^{42–45} More intensive conditioning regimens for eligible patients can overcome the adverse effect of inadequate pre-transplantation response,⁴⁶ but independent multicentre validation has not been done. The debate remains regarding the number of salvage therapies to pursue to reach metabolic complete response before autologous HCT.

The workshop recommendations were that metabolic complete response should be attempted to be reached before autologous HCT using salvage chemotherapy with or without brentuximab vedotin or checkpoint inhibitors. Additionally, autologous HCT is recommended in patients with partial response with low-volume disease if they had received brentuximab vedotin and checkpoint inhibitors as part of the salvage regimen.

What is the role of radiotherapy before or after autologous HCT?

According to the existing literature, peri-transplantation radiotherapy is applied in 10–40% of patients receiving high-dose chemotherapy and autologous HCT for relapsed or refractory Hodgkin lymphoma.^{28,46–51} Its use can be considered particularly in individuals who did not have radiotherapy as part of the first-line treatment, present with a small number of affected sites or bulky disease at relapse, and do not respond sufficiently to systemic salvage therapy or have residual disease after autologous HCT.^{52–54} Insufficient response to systemic therapy and residual lymphoma are both defined by PET-positivity.⁵⁴ If peri-transplantation radiotherapy is considered in patients who already had radiotherapy as a component of frontline treatment, previous radiation volumes and doses should be considered. The decision whether peri-transplantation radiotherapy is applied before or after autologous HCT is made individually, taking into consideration the timing, dose, and duration to avoid any toxicity on engraftment and bone marrow and organ functionality. However, peri-transplantation radiotherapy is more often used after autologous HCT. Advantages of radiotherapy after autologous HCT include potentially smaller radiation volumes as the response to systemic salvage therapy and high-dose chemotherapy is fully defined at that time. Although applied less frequently, radiotherapy before autologous HCT can sometimes be appropriate to reach a better remission status (ie, metabolic complete response) before autologous HCT. Finally, modern radiotherapy techniques have decreased toxicity by reducing irradiated volumes.

the European Group for Blood and Bone Marrow transplantation Practice Harmonisation and Guidelines Committee, Centre Hospitalier Universitaire Lille, University Lille, INSERM U1286, Lille, France (Prof I Yakoub-Agha MD); Clinical Hematology Department, Institut Català d'Oncologia-L'Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain (Prof A Sureda MD)

Correspondence to: Dr Ali Bazarbachi, Bone Marrow Transplantation Program, Department of Internal Medicine, American University of Beirut, 113-6044 Beirut, Lebanon
bazarbac@aub.edu.lb

Detailed information on volumes (mostly the involved site) and doses (depending on the remission status after salvage therapy and before radiotherapy) for peri-transplantation radiotherapy in patients with relapsed or refractory Hodgkin lymphoma undergoing high-dose chemotherapy and autologous HCT is outlined in the guidelines from the International Lymphoma Radiation Oncology Group.^{52,53}

The workshop recommendations were that, when considered, early consultation with a radiation oncologist is recommended, radiotherapy to PET-positive lesions before autologous HCT could be considered, radiotherapy can be considered for patients with persistent PET-positive lesions after autologous HCT, and radiotherapy including a substantial dose to the lungs should be used cautiously.

What is the optimal conditioning regimen before autologous HCT?

There are few randomised studies comparing different conditioning regimens for autologous HCT in Hodgkin lymphoma and the choice is often dictated by centre preference. Carmustine, etoposide, cytarabine and melphalan (BEAM) or lomustine, etoposide, cytarabine, and melphalan (LEAM) is commonly used in Europe. A retrospective UK study of BEAM versus LEAM showed that progression-free survival at 5 years was 49% for BEAM and 54% for LEAM (not significant) with day 100 non-relapse mortality at 3% for BEAM and 2% for LEAM.⁵⁵ In two US studies, busulfan, cyclophosphamide, and etoposide showed lower progression-free survival and higher cumulative incidence of relapse compared with BEAM.^{56,57} Another US retrospective study reported improved progression free survival and overall survival with vorinostat with gemcitabine, busulfan, and melphalan compared with BEAM conditioning.⁴⁶ A randomised phase 2 study of bendaustine-etoposide, cytarabine, and melphalan versus BEAM in mantle cell lymphoma, diffuse large B-cell lymphoma, and follicular lymphoma showed a 1-year progression-free survival rate of 72.5% for bendaustine-EAM and 81.7% for BEAM (not significant), with no superiority of bendaustine-etoposide, cytarabine, and melphalan to BEAM in terms of late lung toxicity.⁵⁸

The workshop found that no prospective randomised trials indicate the superiority of any preparatory regimen over another. However, BEAM is the most frequently used conditioning regimen. It was recommended that, in case of a shortage of carmustine, LEAM or thiotepa (5–7 mg/kg maximum) are an option.

Which patients should receive consolidation or maintenance after autologous HCT? What are the drugs and what is duration? And what is the effect of pre-transplantation use and sensitivity?

Based on the AETHERA trial, candidates for brentuximab vedotin consolidation after autologous HCT are patients

with one or more of the predefined high-risk factors for relapse.^{15,59,60} These high-risk factors include primary refractory disease, relapse within 12 months of first remission, partial response or stable disease as best response to last salvage therapy, extranodal disease at relapse, B symptoms at relapse, and two or more previous salvage therapies. Some factors could be considered especially associated with a poor prognosis; these factors include not having metabolic complete response at the time of transplantation, primary chemoresistance, relapsing within 12 months, and requiring more than one line of rescue therapy. In these cases, one factor could be sufficient to indicate consolidation.

Currently, brentuximab vedotin for up to 16 cycles is the only approved agent for consolidation post-autologous HCT.^{15,59,60} If patients received brentuximab vedotin pre-transplantation, previous doses count toward the 16-cycle limit.⁵⁹ Brentuximab vedotin toxicity might restrict full dose or cycle administration, but real-world data suggest cumulative brentuximab vedotin dose does not affect progression-free survival.⁶¹

Checkpoint inhibitors have been tested in phase 2 trials but are not approved for consolidation or maintenance after autologous HCT.^{62–64} Checkpoint inhibitors include pembrolizumab for eight cycles, nivolumab for up to 6 months, and the combination of brentuximab vedotin plus nivolumab for eight cycles, starting 30–60 days post-autologous HCT. However, the high-risk criteria defined for the brentuximab vedotin plus nivolumab trial were not the same as the AETHERA high-risk criteria.

Off-label checkpoint inhibitors consolidation might be an option in brentuximab vedotin-refractory or brentuximab vedotin-intolerant patients or those previously treated with checkpoint inhibitor-based salvage who reached an optimal response. Other agents, such as lenalidomide or everolimus, have no evidence for their effectiveness as consolidation or maintenance after auto-HCT.

Brentuximab vedotin mainly causes peripheral neuropathy and cytopenia, often requiring dose adjustment or discontinuation. Checkpoint inhibitors are associated with immune-related adverse events, best managed through early recognition and multidisciplinary care.⁶⁵

Importantly, the AETHERA trial enrolled only brentuximab vedotin-naïve patients, and no randomised trials exist in brentuximab vedotin-pretreated patients.¹⁵ Currently, most candidates for autologous HCT have received brentuximab vedotin, and some also received checkpoint inhibitors. Real-world data in series, including brentuximab vedotin-pretreated patients,⁶⁶ show that the disease status at transplantation is the main predictor of progression-free survival, the absence of complete response at transplantation increases the relapse risk, previous brentuximab vedotin exposure does not preclude benefit from consolidation, although efficacy might be reduced. Finally, patients without

complete response might still benefit, but outcomes are superior for those with complete response. No data exists on the effect of previous checkpoint inhibitor exposure or sensitivity on checkpoint inhibitor consolidation.

The workshop found that brentuximab vedotin consolidation in brentuximab vedotin-naïve patients with Hodgkin lymphoma without complete response pre-transplantation or with one or more high-risk factor (following the AETHERA trial) is recommended. The panel supports brentuximab vedotin consolidation in patients with Hodgkin lymphoma with one or more high-risk factor and minimal previous brentuximab vedotin exposure (1–6 cycles), provided that there is no brentuximab vedotin-refractoriness and no previous neurotoxicity. It was recommended that brentuximab vedotin duration should be up to 16 cycles total (including pre-auto-HCT cycles), unless there is unacceptable toxicity or relapse or progression. It was also recommended that off-label checkpoint inhibitor consolidation (ie, pembrolizumab and nivolumab) can be considered in patients with Hodgkin lymphoma with high-risk factors and brentuximab vedotin-refractory disease or brentuximab vedotin-intolerant disease; however, the benefit should be weighed against potential immune-related side-effects. Finally, off-label consolidation with brentuximab vedotin plus checkpoint inhibitors can be considered in patients who are not refractory and not intolerant to brentuximab vedotin; however, the benefit should be weighed against potential immune-related side-effects.

Allogenic HCT

Which patients are candidates for allogenic HCT?

For a long time, allogenic HCT was the only potentially curative treatment for patients who relapse after autologous HCT and is still recommended as standard of care in this setting.² Outcomes after allogenic HCT have substantially improved over time⁶⁷ but numbers of transplantations are decreasing because a higher percentage of patients are cured after frontline treatment and first relapse. In the last 5 years, treatment of relapse after autologous HCT relied on brentuximab vedotin and checkpoint inhibitors. Despite a high response rate, progression-free survival is short except in patients reaching complete response.^{16–18} For patients who reach complete response, recent data suggest that allogenic HCT can be deferred in patients who relapse after autologous HCT but reach complete response with brentuximab vedotin or checkpoint inhibitors.⁶⁰ For patients who do not reach complete response, although some studies suggest durable clinical benefit from checkpoint inhibitor therapy that extends beyond radiographical progression, most of these patients are relatively young, and prolonged treatment aimed solely at slowing disease progression, without a realistic expectation of cure, might not represent an optimal long-term strategy. In such cases, allogenic HCT remains the only potentially curative option.

Emerging recognition of inborn errors of immunity indicates that a subset of adolescents and young adults with Hodgkin lymphoma, particularly those relapsing after autologous HCT, might have underlying immune dysregulation. In such patients, allogenic HCT can offer benefit by both controlling lymphoma and correcting the immune defect. Evaluation for inborn errors of immunity should be considered when clinical features are suggestive.^{68,69}

The workshop found that consolidation with allogenic HCT is recommended for eligible patients post-brentuximab vedotin and post-checkpoint inhibitor exposure (eligibility is defined as relapse after autologous HCT, adequate organ function, physical conditions including performance status, and sensitive disease before allogenic HCT). Additionally, it was found that allogenic HCT can be postponed in patients with complete response post-checkpoint inhibitors as many of these patients can reach long-lasting remissions. For refractory patients, decision to allograft should be done on an individual basis. It was recommended that the time interval between the last dose of checkpoint inhibitors and allogenic HCT is preferably at least 6 weeks, if clinically feasible. Furthermore, clinicians should consider the use of bridging therapy before allogenic HCT to reduce the risk of relapse.

Transplantation modalities of allogenic HCT in patients with Hodgkin lymphoma?

With the availability of reduced intensity conditioning and haploidentical transplants, non-relapse mortality was substantially reduced and almost all patients have a donor except some non-white patients who have a lower chance to find an unrelated donor. In the allogenic HCT setting, age and disease status are major determinants for progression-free survival and overall survival, HLA-matched donors and reduced intensity conditioning yield the best outcomes.^{67,70} The superiority of HLA-matched donors over haploidentical donor with post-transplant cyclophosphamide (PTCy) has not been uniformly shown.⁷¹

Both brentuximab vedotin and checkpoint inhibitors can be safely used before allogenic HCT and produced excellent results.^{19–22} However, historically, several studies reported higher than normal rates of early severe acute GVHD^{20,21,72} and these results prompted a warning from the US Food and Drug Administration to use caution when using checkpoint inhibitors as a bridge to allogenic HCT. A longer than 6 weeks duration between the last checkpoint inhibitor exposure and the transplantation and the use of PTCy for GVHD prophylaxis, regardless of the type of donor, were both associated with better outcomes.⁷³ Although the conventional PTCy regimen of 50 mg/kg per day on days 3 and 4 after transplantation is most widely used, alternative approaches using reduced doses have been explored with the aim of mitigating toxicity while preserving efficacy. The 2025 joint registry

data from EBMT and The Center for International Blood and Marrow Transplant Research showed that previous exposure to checkpoint inhibitors is associated with increased progression-free survival due to decreased relapse after allogeneic HCT,²² suggesting increased graft versus lymphoma.

Donor selection is recommended in the following order: HLA-matched sibling donor, HLA-matched unrelated donor, and HLA-haplo identical donor or HLA-mismatched unrelated donor (reduced intensity conditioning using PTCy for both); cord blood should be avoided in adults unless no alternative donor is available. Regarding the condition regimen, reduced intensity conditioning (such as fludarabine-melphalan, fludarabine and busulfan for 2 days, or fludarabine plus cyclophosphamide plus total body irradiation) is preferred. In patients at high risk of relapse (such as those with no metabolic complete response), conditioning regimens with higher intensity (but reduced organ toxicity) can be considered (eg, thiotepa for 1 day, busulfan for 2 days, and fludarabine-T1B2F). BEAM-based conditioning could be considered if allogeneic HCT was used for the first transplant. PTCy is the recommended GVHD prophylaxis independently of the donor type (particularly in checkpoint inhibitor pre-treated patients). Other methods of T-cell depletion (eg, antithymocyte globulin or alemtuzumab plus donor lymphocyte infusion [DLI]) could be considered for HLA identical siblings or unrelated donor.

How to prevent and manage relapse after allogeneic HCT?

Data on brentuximab vedotin maintenance after allogeneic HCT are scarce with no definitive efficacy established. Similarly, no definitive data are available for checkpoint inhibitor maintenance. Early immunosuppression tapering and discontinuation is not recommended due to increased risk of severe GVHD. DLI can induce durable remissions when used pre-emptively, but responses are inconsistent and GVHD risk remains considerable. Novel approaches, such as circulating tumour DNA (ctDNA) and thymus and activation-regulated chemokine (TARC) monitoring, are promising for relapse prediction but have little standardisation and validation in the post-allogeneic HCT setting. At present, no routine maintenance therapy can be recommended as standard of care following allogeneic HCT in Hodgkin lymphoma. Novel biomarker-driven surveillance remains investigational. Clinical trial participation and individualised, risk-adapted strategies currently represent the most appropriate approach for managing patients with high-risk Hodgkin lymphoma after allogeneic HCT.

Treatment of relapse after allogeneic HCT typically involves a combination of approaches to control the disease and improve outcomes. Commonly used strategies include DLI, which can induce remission in around 50% of cases. Brentuximab vedotin is effective treatment for relapsed or refractory Hodgkin lymphoma

and can be effective post-allo-HCT relapse.²³ Checkpoint inhibitors (ie, nivolumab and pembrolizumab) have shown promising activity post-transplantation.^{24,25} It is preferable to start checkpoint inhibitors at a low dose with gradual dose escalation in the absence of response and toxicity to minimise the risk of GVHD. Patients should also be carefully monitored for early signs of GVHD. Salvage chemotherapy can be used to reduce disease burden before other treatments. Chemotherapy, immunotherapy, and brentuximab vedotin with or without DLI can be combined. Finally, radiotherapy can be used for localised disease control or palliation.

In select cases, a second allogeneic or autologous transplant could be considered, especially if remission was reached with previous therapies. Early-phase trials showed safety and anti-tumour response of CD30-directed CAR T-cells in relapsed or refractory Hodgkin lymphoma, including post-allo-HCT settings, and further trials are needed to confirm efficacy and durability.⁷⁴

All treatment decisions should be individualised based on patient performance status, disease characteristics, previous treatments, and availability of clinical trials. A personalised approach, often beginning with immunotherapy or targeted agents, followed by consideration of cellular therapies (eg, DLI) or second transplant in suitable candidates is recommended. Autologous HCT is generally not recommended after failure of allogeneic HCT.

The workshop found that there is no recommendation for maintenance therapy after allo-HCT outside of clinical trials. More clinical trials and new biomarkers need to be developed before a recommendation on maintenance therapy can be made. The recommended treatment for relapse includes the following: tapering immunosuppression treatment, DLI with or without brentuximab vedotin (checkpoint inhibitors should be used with caution), chemotherapy, brentuximab vedotin, checkpoint inhibitors used with caution, and radiotherapy, which can be considered for patients with persistent PET-positive lesions after allo-HCT, as well as more prospective clinical trials including trials on cellular therapy.

Unanswered questions and further research

Several clinically relevant questions remain unresolved and are being addressed through ongoing clinical trials. These include the role of PET-CT before autologous HCT in guiding post-transplantation consolidation strategies, and the necessity of autologous HCT in patients reaching metabolic complete response after checkpoint inhibitor-based salvage. Another area of investigation is the role of allogeneic HCT as a first transplantation strategy in patients who have not responded to chemotherapy, brentuximab vedotin, or checkpoint inhibitor therapy. In addition, the role of maintenance therapy following allogeneic HCT is yet to be established. Finally, the integration of innovative biomarkers, such as ctDNA for

Search strategy and selection criteria

A systematic literature search was conducted of PubMed and abstracts of meeting proceedings (including the European Society for Blood and Marrow Transplantation, the American Society of Hematology, the American Society of Clinical Oncology, the International Conference on Malignant Lymphoma, the American Society for Transplantation and Cellular Therapy, and the Center for International Blood and Marrow Transplant Research meetings) published in English between Jan 1, 2000, and Dec 15, 2025, with key terms such as “Hodgkin lymphoma”, “treatment strategies”, and “haematopoietic stem-cell transplantation”. The European Society for Blood and Marrow Transplantation Registry data were used. Relevant papers were included based on the authors' opinion.

minimal residual disease assessment and TARC, into routine clinical practice represents a promising but still evolving field. These tools have the potential to improve response assessment and enable more precise patient stratification for autologous HCT, allogenic HCT, or maintenance strategies, although their standardisation and prospective validation are still required.

Contributors

AS and AB are the leaders of this workshop. AS and AB conceived and designed the manuscript topics. All authors contributed to the literature review, data interpretation, formulation of recommendations, and preparation of the panels. AB and IY-A formatted the final version of the manuscript. IY-A wrote the abstract and tables. All authors played an important role in drafting the recommendations, revising the manuscript, approving the final version, and agreeing to be accountable for all aspects of the work to ensure that any issues related to accuracy or integrity are properly investigated and resolved. All authors contributed equally to this work.

Declaration of interests

AB has participated in a speaker bureau or on the advisory board for Novartis, Roche, Sanofi, Jazz, Adienne, Astellas, Takeda, Hikma, Janssen, MSD, Abbvie, Pfizer, and Amgen and has received research support from Novartis, Roche, Takeda, Janssen, Astellas, Biologix, Pfizer, and Amgen. RA is the Chair of NCCN Hodgkin lymphoma committee and has received institute research funding from Merck and Seattle Genetics (Pfizer). SA has received research support to their institution for clinical trials from Nektar, Merck, Genmab, KITE/Gilead, Janssen, Bristol Myers Squibb, and Caribou and is a consultant for ADC therapeutics, KITE/Gilead, Genmab, and Bristol Myers Squibb. MH reports consultancy fees from Caribou, Autolus, Forte Biosciences, Byondis, Daiichi Sankyo, Bristol Myers Squibb, Caribou, Kite, Incyte, and Abbvie; has participated on an advisory board for CRISPR; and has participated in a speaker's bureau for AstraZeneca, ADC Therapeutics, BeiGene, Kite, and Sobi. CM is an advisory board member and reports speaker's honorary and travel grants for Takeda. M-AP reports honoraria from Allogene, Cartesian, Celgene, Bristol-Myers Squibb, Incyte, Kite/Gilead, MSD, Miltenyi Biotec, Nektar Therapeutics, Novartis, Ossium Health, Pierre Fabre, Sanofi, and Takeda; serves on the data safety monitoring board for Cidara Therapeutics and Sella Life Sciences; has received institutional research support for clinical trials from Allogene, Genmab, Incyte, Kite/Gilead, Miltenyi Biotec, Novartis, and Trlx; is a member and on the board of directors for The National Marrow Donor Program (unpaid position); and has ownership interests in Omeros and OrcaBio, neither of which are considered relevant conflicts to the present guidelines publication. Omeros was granted approval by the US Food And Drug Administration for narsoplimab to treat transplant-associated thrombotic

microangiopathy and narsoplimab is not indicated for patients with Hodgkin lymphoma unless they have transplant-associated thrombotic microangiopathy. Orcabio's lead drug, OrcaT (an engineered hematopoietic cell graft) is currently under review for approval by the US Food and Drug Administration, and would not be used in patients with Hodgkin lymphoma. LS reports advisory board member participation, speaker's honorary, and travel grants for Kyowa Kirin; royalties for Springer Verlag and Munksgaard Publishing; research grants for Danish Cancer Society; is the vice-chairman for International Lymphoma Radiation Oncology Group; and is a board member and chairman of radiotherapy subcommittee for Danish Lymphoma Group. FO participated in speakers bureaus for Takeda, Kyowa Kirin, Menarini Stemline, Johnson and Johnson; reports support for travel for Takeda, Kyowa Kirin, Johnson and Johnson, and Roche; and is the Chair of the data safety monitoring board for the DKMS GRAPPA trial (ongoing). MAN reports consulting fees, support for travel for Takeda and payment or honoraria for lectures for Takeda and Bristol Myers Squibb. IY-A is the current chair of the European Group for Blood and Bone Marrow transplantation practice harmonisation and guidelines committee; reports payment or honoraria for lectures for Novartis, Kite/Gilead, and Bristol Myers Squibb. AS reports consultancy fees from Takeda, BMS Celgene, Novartis, Janssen, Gilead, and Sanofi; participation in a speakers Bureau from Takeda; reports speaker honoraria from Takeda, BMS/Celgene, MSD, Janssen, Amgen, Novartis, Gilead Kite, Sanofi, Roche, and Alexion; and research support from Takeda and BMS Celgene. All other authors declare no competing interests. The European Group for Blood and Bone Marrow transplantation is a non-profit medical and scientific organisation. The European Group for Blood and Bone Marrow transplantation performed administrative and legal management, as well as funding acquisition. No pharmaceutical company and no other funding source were involved in any way or had a role in the study design, data collection, data analysis, data interpretation, or writing of this Review. No medical writer or editor was involved.

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