Annals of Hematology (2019) 98:1973–1980
https://doi.org/10.1007/s00277-019-03704-z

ORIGINAL ARTICLE

BAM conditioning before autologous transplantation for lymphoma: a study on behalf of the Francophone Society of Bone Marrow Transplantation and Cellular Therapy (SFGM-TC)

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Received: 20 November 2018 / Accepted: 21 April 2019 / Published online: 20 May 2019

Abstract

High-dose chemotherapy before autologous transplantation is a therapeutic option as consolidation in primary or relapsed lymphoma. Even if BEAM conditioning is generally used, alternative conditioning regimens have been published. The purpose of this study was to assess the outcome of 177 adult patients with lymphoma whose conditioning treatment included a BAM (busulfan, aracytine, and melphalan) regimen. With a median follow-up of 17.4 months, 2-year estimates of overall survival and progression-free survival for the entire group were 87% and 70.5%, respectively. Mucositis was the main reported complications and infectious episodes were described in 80.2% of patients. According to multivariate analysis, high performance status and age at diagnosis were adverse factors for survival and increased the risk of disease relapse and death. Despite its limitations, this retrospective study suggests that BAM combination is a valid conditioning regimen in lymphoma patients, with an acceptable rate of toxicity.

Keywords Autologous transplantation · Conditioning regimen · BEAM · BAM · Lymphoma

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00277-019-03704-z) contains supplementary material, which is available to authorized users.

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Introduction

Despite advanced non-Hodgkin lymphomas (NHL) and Hodgkin lymphomas (HL) being considered as chemotherapy-sensitivity tumors, many patients relapse or are never in remission (R/R) after standard induction treatment. These situations are associated with poor outcome and necessitate other therapeutics. High-dose chemotherapy supported by autologous hematopoietic stem cell transplantation (ASCT) is the preferred therapeutic option for R/R lymphoma patients, considering that both disease-free and overall survival are improved in patients with chemosensitive-relapsed lymphomas [1–7].

Adequate conditioning regimen is important to optimize better control of R/R NHL and HL with the aim to target residual malignant cells with minimal toxicity [4–6]. The choice of regimen is based on institutional experience. BEAM (carmustine (BICNU), etoposide, cytarabine, and melphalan) conditioning is usually the preferred regimen for the treatment of R/R NHL and HL [2, 7]. Recently, BICNU was in short supply in French centers. Moreover, BICNU has a high cost and BEAM or other carmustine-containing regimens are not a good option for all physicians around the world. With regard to these situations, alternative regimens are needed.

In this context, the Francophone Society of Bone Marrow Transplantation and Cellular Therapy (SFGM-TC) and the Lymphoma Study Association (LYSA) established a collaborative working group to discuss alternative regimen to BEAM. Different conditioning or drug options were discussed. However, as no prospective comparative studies were done, it has been difficult to preferentially recommend one conditioning regimen or another [8, 9].

Little is known regarding the use of different specific regimens, in particular for BAM (busulfan, aracytine, and melphalan) conditioning [10, 11]. Based on these considerations, the SFGM-TC/LYSA collaborative working group has proposed to evaluate different regimens to update data. In this study, we conducted a retrospective analysis of all patients treated in the SFGM register participating centers between 2000 and 2015 with BAM conditioning before ASCT.

Patients and methods

Patients

We identified 177 French patients treated between 2000 and 2015. Inclusion criteria were age less than 70 years, Hodgkin or non-Hodgkin lymphomas, and BAM conditioning used for a first ASCT. Data were retrospectively collected from the ProMISe (Project Manager Internet Server) database with a second check in all patients' files. Histological diagnosis was based on local review.

Transplantation procedures

Conditioning-associated busulfan per os (4 mg/kg/day) or intravenous (3.2 mg/Kg/day) for three consecutive days, cytarabine 6 g/m^2 total dose and melphalan 140 mg/m^2. In practice, the median dose for busulfan was 700.8 mg [590.4–792.0], 11.3 g [10.2–12.0] for cytarabine, and 257.6 mg [231.7–280.0] for melphalan. All grafts were peripheral blood stem cells (PBSC). The median infused cell dose was 4.79×10^6 CD34+/Kg (min 1.53; max 19.86). Medical care after transplantation was provided in accordance with the centers' practices.

Definition and evaluation

Outcomes included neutrophil and platelet engraftment, progression-free survival (PFS), non-relapse mortality (NRM), and overall survival (OS). Time to neutrophil engraftment was defined as the first of three consecutive days on which neutrophils exceeded 0.5×10^9/L. Time to platelet engraftment was defined as the first of three days with 20×10^9/L platelets without platelet transfusion during a 5-day period. Disease progression or relapse (if complete remission had been achieved before ASCT) was defined by reappearance of signs of the disease with cytology or histology confirmation. We designated NRM as death from any cause without evidence of relapse/progression of the disease. OS was calculated from the date of ASCT to the date of death from any cause and censored at the date of the last follow-up. PFS was calculated from ASCT date to disease progression or death (regardless of cause of death), whichever comes first. Toxicities including mucositis, infection, cardiac, pulmonary, gut, or other complications were retrospectively graded according to Common Terminology Criteria for Adverse Events (CTCAE). Febrile neutropenia without documentation was denied by the onset of isolated fever, in absence of local inflammation evocative for clinical infection, and without microbial documentation of the episode.

Statistical analysis

Patient, disease, and treatment characteristics were summarized with continuous variables described by median and range as well as categorical variables described by frequency and percentage. All survival durations were measured from the date of treatment to the date of event or the date of the last contact (censored data). The probability of OS and PFS was calculated using Kaplan–Meier estimator and the log-rank test was used for univariate comparisons. Hazard ratios and 95% confidence intervals were estimated. Hazard ratios for NRM were calculated using the subdistribution hazards model to accommodate competing risks and univariate comparison was made using the Fine–

Table 1 Baseline characteristics of patients

Characteristics	$N = 177$
Median age of patients, yr. (range)	51.9 (38.0–60.1)
Gender of patients	
Male	122 (68.9)
Female	55 (31.1)
Diagnosis	
NHL	147 (83.1)
Hodgkin	23 (13.0)
Lymphoma WHO classification (2015)	
DLBCL	53 (29.9)
Mantle cell lymphoma	41 (23.2)
Hodgkin	25 (14.1)
Low grade NHL	26 (14.7)
T cell lymphoma	16 (9.0)
B cell lymphoma, NOS	8 (4.5)
Burkitt lymphoma	8 (4.5)
Performance status	
ECOG 0–1	145 (81.9)
ECOG ≥ 2	3 (1.6)
Unknown	29 (16.4)
Comorbidities	
No	131 (74.0)
Yes	33 (18.6)
Prior solid tumor	15 (8.5)*
Diabetes requiring treatment	14 (7.9)
Infection at transplantation	1 (0.6)
unknown	13 (7.3)
Median interval from diagnosis to transplantation, days (range)	272 (172.5–760)
Number of lines before transplantation	
1	80 (45.2)
2	81 (45.8)
3 or more	11 (6.2)
Unknown	5 (2.8)
Previous monoclonal antibodies	
No	38 (21.5)
Yes	126 (71.2)
Unknown	13 (7.3)
Previous radiotherapy	
No	146 (82.5)
Yes	17 (9.6)
Unknown	14 (7.9)
Disease status at transplantation	
CR	113 (63.8)
PR	47 (26.6)
Relapse	7 (4.0)
Progression	5 (2.8)
Unknown	5 (2.8)
BAM conditioning regimen	
Median dose of ARA-C/cytarabine, g (range)	11. 3 (10.2–12.0)
Median dose of busulfan, mg (range)	700.8 (590.4–792.0)
Median dose of melphalan, mg (range)	257.6 (231.7–280.0)

Values are total number of cases with percent in parentheses, unless otherwise noted

NHL, non-Hodgkin lymphoma; *DLBCL*, diffuse large B cell lymphoma; *NOS*, not otherwise specified; *PS*, performance status; *CR*, complete remission; *PR*, partial remission; *BAM*, busulfan-aracytin-melphalan. Comorbidities were defined according to the EBMT forms registry (prior solid tumor, inflammatory bowel disease, rheumatologic, lupus nephritis, infections, diabetes, gonadal dysfunction, growth impairment, other)

*Patients might have multiple solid tumors

Gray model. Multivariable analyses were performed using Cox proportional hazards regression or the Fine–Gray method. Variables with univariate $P \leq 0.2$ were entered into the multivariate model with subsequent application of a model selection algorithm. Backward elimination procedure based on AIC criteria was used to select significant covariates. Interactions between significant covariates were examined. All calculations were performed using R software (version 3.2.5). Statistical significance was set at $P < .05$ level; all P values were two-sided.

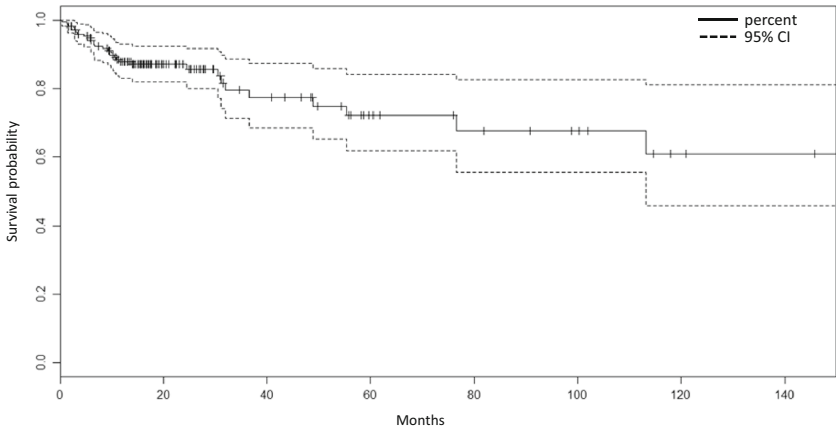

Fig. 1 Kaplan–Meier probability of overall survival after ASCT with BAM conditioning. The 3-year OS rate was 74% and the median OS was not reached

Results

Patient characteristics

Patient demographics and disease characteristics are presented in Table 1. A total of 177 patients were included. The median age at diagnosis was 51.9 years (range, 38.0–60.1). The median time from diagnosis to ASCT was 272 days (range, 172.5–760). Indications for transplantation were diffuse large B cell lymphoma (DLBCL) (29.9%), mantle cell lymphoma (MCL) (23.2%), Hodgkin's lymphoma (HL) (14.1%), low-grade NHL (14.7%), T cell lymphoma (9%), B cell lymphoma non-specified (4.5%), and Burkitt lymphoma (4.5%). For the 136 B cell lymphomas, 126 received rituximab before ASCT. Only 17 patients received prior radiotherapy before ASCT. The median number of treatment before ASCT was 2 (range, 1–5). Patients received 1 (45.2%), 2 (45.8%), 3, or more (6.2%), unknown (UK) (2.8%) treatment lines before ASCT. At time of transplantation, disease status was complete remission (63.8%), partial remission (26.6%), relapse (4.0%), progression (2.8%), or UK (2.8%) (Table 1).

Transplant-related toxicity

During neutropenia period, mucositis occurred in 130 patients (78.5%). The WHO toxicity grading was 2 (33.1%), 3 (36%) and 4 (19.4%). Moreover, infectious complications were described in 142 patients (80.2%). Febrile neutropenia without documentation was the principal diagnosis (60.6%). Other complications were pneumonia (15.5%), sepsis (9.2%), gut infections (4.9%), catheter infection (4.9%), urinary tract (2.8%), or unknown (2.1%). Digestive complications were described in 135 patients (76.3%). Seventy-two patients (40.7%) presented with diarrhea or colitis with a maximum toxicity grading of 1–2 (23.7%), or grade ≥ 3 (14.1%). The median duration was 7 days (range, 5–10). Pulmonary toxicity (different from pneumonia) was reported in 12 patients (6.8%), with 8 cases of respiratory distress syndrome. No detail was provided for the reason in these cases. Two cases were fatal, one of those occurred more than 6 months after ASCT and salvage treatment for subsequent relapse/progression. An overview of the main extra-hematological toxicities is detailed in Supplementary Table 1. In the first 100 days, 10 patients

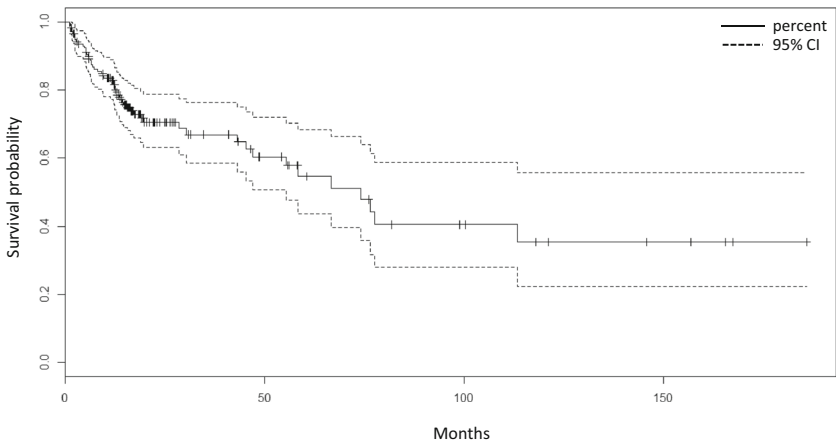

Fig. 2 Kaplan–Meier probability of progression-free survival after ASCT with BAM conditioning. The 3-year PFS rate was 65.2% and the median PFS was 71.5 months

Table 2 Univariate analysis for OS, PFS, and NRM

Variable	OS			PFS			NRM		
	HR	95% CI	*P* value	HR	95% CI	*P* value	SH	95% CI	*P* value
Age	1.03	1.01–1.06	0.008*	1.03	1.01–1.04	0.003*			
< 40							1.00		
40–60							1.73	0.32–9.26	0.52
> 60							2.15	0.37–12.4	0.39
Gender			0.855			0.869			0.45
Female	1.00			1.00			1.00		
Male	0.93	0.43–2.00		1.05	0.59–1.87		1.77	0.4–7.86	
Diagnosis			0.202			0.479			0.72
Hodgkin	1.00			1.00			1.00		
NHL	2.29	0.54–9.65		1.36	0.58–3.18		1.42	0.21–9.8	
Performance status			< 0.001*			0.007*			0.0025*
ECOG 0–1	1.00			1.00			1.00		
ECOG ≥ 2	4.84	1.82–12.89		2.84	1.29–6.27		6.43	1.26–32.68	
Comorbidities			0.201			0.473			0.0028*
No	1.00			1.00			1.00		
Yes	1.75	0.73–4.17		1.28	0.65–2.5		8.26	2.06–33.01	
Number lines of treatment			0.255			0.853			
1	1.00			1.00			1.00		
2	1.82	0.78–4.23		1.17	0.66–2.06		1.84	0.32–10.57	0.5
3 or more	2.49	0.66–9.38		1.2	0.41–3.5		3.12	0.4–24.09	0.27
Previous monoclonal Ab			0.018*			0.047*			0.31
No	1.00			1.00			1.00		
Yes	0.41	0.19–.88		0.55	0.3–1.0		0.49	0.12–1.93	
Previous radiotherapy			0.189			0.748			
No	1.00			1.00			1.00		0.057
Yes	1.85	0.73–4.68		0.87	0.38–2.0		3.62	0.96–13.6	
Pre-transplant disease status			0.38			0.67			
CR	1.00			1.00			1.00		
PR	1.38	0.6–3.16		1.28	0.71–2.32		0.44	0.05–3.92	0.46
Relapse or progression	2.1	0.74–5.98		1.26	0.53–2.96		1.9	0.34–10.49	0.46
Number of the disease status			0.583			0.627			
First	1.00			1.00			1.00		
Second	1.2	0.55–2.65		0.78	0.42–1.45		0.84	0.17–4.16	0.83
Third or more	2.09	0.48–9.08		1.29	0.4–4.2		3.54	0.77–16.19	0.1

Ab, antibodies; *NHL*, non-Hodgkin lymphoma

died with 2 cases of relapse and 3 cases related to toxicity (1 respiratory distress and 2 multivisceral failures). For the 5 other cases, causes of death were not documented. Secondary cancers were described in 7 patients (4% of the total population) (2 lung cancers, 1 epidermoid cancer, 2 pancreatic cancers, 1 finger adenocarcinoma, and 1 leukemia). However, no death was due to secondary neoplasia in the study period. The cumulative incidence of NRM was 3.03% at 24 months.

Post-transplant outcomes

Engraftment was effective for 175 patients. For all these patients, neutrophil recovery was described with a median time of 11 days (range, 10–12). Median time of platelet ($> 20.10^9$/L) recovery was 13 days (range, 11–17). Median follow-up was 17.4 months (range, 11.7–30.5). At the end of the follow-up, 145 patients (81.9%) were alive and 42 (23.7%) patients had relapsed. Cumulative incidence of relapse or progression

Table 3 Multivariate analysis for OS, PFS, and NRM

Variable	OS			PFS			NRM		
	HR	95% CI	*P* value	HR	95% CI	*P* value	SH	95% CI	*P* value
Performance status			0.022*			0.034*			0.004*
ECOG 0–1	1.00			1.00			1.00		
ECOG ≥ 2	4.07	1.32–12.53		2.59	1.15–5.83		15.73	2.38–103.83	
Number lines of treatment			0.058			–			–
1	1.00			–	–		–	–	
2	3.4	1.15–10.1		–	–		–	–	
3 or higher	1.02	0.11–9.62		–	–		–	–	
Previous monoclonal antibodies			0.021*			0.09			–
No	1.00			1.00			–	–	
Yes	0.28	0.1–0.79		0.52	0.25–1.07		–	–	
Age at diagnosis	1.1	1.04–1.17	< 0.001*	1.04	1.01–1.07	0.003*	–	–	–

was 5.4% at 3 months and 15.6% at 12 months. Relapse rates at 2 years were 22.0%, 23.2%, and 28.6%, for the whole cohort, Hodgkin lymphoma, and non-Hodgkin lymphoma, respectively. At the end of the study, the main causes of death were disease progression ($n = 16$, 9.0%) and toxicity (after ASCT or after treatment of relapse) ($n = 10$, 5.6%). The median OS was not reached and the median PFS was 74 months (range, 55.3—NR) (Figs. 1 and 2). The 2-year OS rate was 87% and 70.5% for the 2-year PFS rate.

We evaluated factors influencing outcomes of the cohort. Details are presented in Tables 2 and 3. In univariate analysis, performance status (ECOG ≥ 2 vs 0–1), previous monoclonal antibodies (yes vs no) therapy, and age at diagnosis were the only factors that predicted survival (Table 2). None of the other characteristics listed in Table 1 were significant predictors of OS and PFS. The multivariate analysis for the OS, PFS, and NRM showed that performance status ECOG ≥ 2 is associated with a worst outcome (OS: HR, 4.07; $P = 0.022$; PFS: HR, 2.59; $P = 0.034$) (Table 3). Age at diagnosis has also an influence on the survival (OS: HR, 1.1; $P = <0.001$; PFS: HR, 1.04; $P = <0.003$). Of note, these outcomes were not affected by the disease sub-type either on univariate or multivariate analysis.

Discussion

In this work, we found that BAM regimen used in lymphoid malignancies is of acceptable toxicity (hematologic and digestive), with a constant hematopoietic recovery. Even if BEAM regimen is the most used conditioning regimen, few data are available comparing this regimen with other possibilities [7, 12–15]. Discussion is still ongoing to elect relevant therapeutic options combining better association of drugs for the disease control with less toxicity [6, 16]. Little data, especially prospective studies, were published while comparing different alternatives. Recently, we have proposed an exhaustive review of these alternative possibilities [12]. Interestingly, BAM regimen is a well-known conditioning for ASCT but unfortunately, very few data are available with only two studies published to date [10, 11]. While the main objective of the first study was the feasibility of the use of fresh low dose of CD34+ cells infusion [15], the second study focused on the usage of BAM regimen for unfavorable Hodgkin disease as the second part of multiple transplant programs [14]. We focused our discussion in comparison with BEAM conditioning because it is probably better described in the literature.

Little is known regarding BAM toxicity [11]. Mucosal toxicity is a common complication of busulfan, melphalan, and cytarabine chemotherapies. Accordingly, in our cohort, mucositis was the most important adverse effect and we depicted a similar incidence of colitis as compared to BEAM regimen [6, 7, 12–14, 17]. The incidence of febrile neutropenia (60.6%) was comparable to those described with BEAM (67%) or ByCyE (77%) conditioning (18). We have also found that 12 patients (6.8%) presented pulmonary symptoms, including 8 patients with distress syndrome. Pulmonary toxicity has not been well-documented in studies related to BEAM regimen, except for pulmonary fibrosis that has been previously linked to busulfan. This type of complication has not been monitored in the present study. In our cohort, one pulmonary fatal case was described after treatment of relapse after ASCT but was probably not related directly to ASCT. With two alkylating agents in the conditioning regimen and high-dose chemotherapy, sinusoidal obstruction syndrome (SOS) was also a complication to monitor. Despite heavy treatment before transplantation, only 2 patients presented non-fatal SOS. Overall, NRM at 12 months was estimated at 3.03%. This result is similar after BEAM ASCT [9, 18]. However, caution has to be made for secondary neoplasia as few data are available

after autologous transplantation. In fact, we have noted seven secondary cancers (4%) with a short follow-up; no death was attributed of secondary cancer. Bhatia and co-workers previously described late mortality with 7% of death because of secondary cancers. However, different hematological diseases were studied and no details of conditioning were provided [18]. Overall, our results did not differ as compared to published data for other conditioning, even though our study is retrospective with a short follow-up.

Engraftment was efficient with rapid neutrophil (11 days) and platelets (13 days) reconstitution. Despite short follow-up, OS and PFS at 2 years were similar with BEAM-conditioning data in the literature [2, 5, 6, 14, 15, 17, 18]. Best results were noted for patients with fewer lines of treatment before transplantation and if performance status was good. The number of lines of treatment might also be biased, depending whether one could consider a refractory status before transplantation either with multiple lines of treatment or with a single line of treatment to achieve a treatment response. It is also noteworthy to consider that, even though practice (e.g., oral busulfan or intravenous injection), indications or supportive care has changed during the timeframe of the study. The majority of patients were indeed treated in the recent period of time, with 119 patients from 2013 to 2015.

In conclusion, BAM conditioning before ASCT is probably a good alternative in the treatment of lymphomas. Disease control seemed correct without an excess toxicity. Further studies, including extended follow-up and prospective cohorts, are therefore needed in order to compare BAM and BEAM-conditioning regimens and to draw conclusive reports.

Compliance with ethical standards

Conflict of interest EG received research support from Pierre Fabre. The remaining authors declare that they have no conflict of interest.

Ethical approval This study was approved by the SFGM-TC scientific council and performed according to the SFGM-TC guidelines and in accordance with the principles of the declaration of Helsinki.

Informed consent Informed consent was obtained from all subjects.

References

1. Philip T, Guglielmi C, Hagenbeek A, Somers R, van der Lelie H, Bron D, Sonneveld P, Gisselbrecht C, Cahn JY, Harousseau JL, Coiffier B, Biron P, Mandelli F, Chauvin F (1995) Autologous bone marrow transplantation as compared with salvage chemotherapy in relapses of chemotherapy-sensitive non-Hodgkin's lymphoma. N Engl J Med 333:1540–1545. https://doi.org/10.1056/NEJM199512073332305
2. Mills W, Chopra R, McMillan A, Pearce R, Linch DC, Goldstone AH (1995) BEAM chemotherapy and autologous bone marrow transplantation for patients with relapsed or refractory non-Hodgkin's lymphoma. J Clin Oncol Off J Am Soc Clin Oncol 13:588–595. https://doi.org/10.1200/JCO.1995.13.3.588
3. Andre M, Henry-Amar M, Pico JL et al (1999) Comparison of high-dose therapy and autologous stem-cell transplantation with conventional therapy for Hodgkin's disease induction failure: a case-control study. J Clin Oncol 17(1):222–229. https://doi.org/10.1200/JCO.1999.17.1.222
4. Fernandez HF, Escalón MP, Pereira D, Lazarus HM (2007) Autotransplant conditioning regimens for aggressive lymphoma: are we on the right road? Bone Marrow Transplant 40:505–513. https://doi.org/10.1038/sj.bmt.1705744
5. Chen Y-B, Lane AA, Logan BR, Zhu X, Akpek G, Aljurf MD, Artz AS, Bredeson CN, Cooke KR, Ho VT, Lazarus HM, Olsson RF, Saber W, McCarthy PL, Pasquini MC (2015) Impact of conditioning regimen on outcomes for patients with lymphoma undergoing high-dose therapy with autologous hematopoietic cell transplantation. Biol Blood Marrow Transplant 21:1046–1053. https://doi.org/10.1016/j.bbmt.2015.02.005
6. Salar A, Sierra J, Gandarillas M, Caballero MD, Marín J, Lahuerta JJ, García-Conde J, Arranz R, León A, Zuazu J, García-Laraña J, López-Guillermo A, Sanz MA, Grañena A, García JC, Conde E, GEL/TAMO Spanish Cooperative Group (2001) Autologous stem cell transplantation for clinically aggressive non-Hodgkin's lymphoma: the role of preparative regimens. Bone Marrow Transplant 27:405–412. https://doi.org/10.1038/sj.bmt.1702795
7. Jo J-C, Kang BW, Jang G, Sym SJ, Lee SS, Koo JE, Kim JW, Kim S, Huh J, Suh C (2007) BEAC or BEAM high-dose chemotherapy followed by autologous stem cell transplantation in non-Hodgkin's lymphoma patients: comparative analysis of efficacy and toxicity. Ann Hematol 87:43–48. https://doi.org/10.1007/s00277-007-0360-0
8. Damaj G, cornillon J, Bouabdallah K et al (2017) Carmustine replacement in intensive chemotherapy preceding reinjection of autologous HSCs in Hodgkin and non-Hodgkin lymphoma: a review. Nature Publishing Group, London, pp 1–9. https://doi.org/10.1038/bmt.2016.340
9. Isidori A, Christofides A, Visani G (2016) Novel regimens prior to autologous stem cell transplantation for the management of adults with relapsed/refractory non-Hodgkin lymphoma and Hodgkin lymphoma: alternatives to BEAM conditioning. Leuk Lymphoma 57:2499–2509. https://doi.org/10.1016/S0140-6736(15)60165–9
10. Brice P, Divine M, Simon D, Coiffier B, Leblond V, Simon M, Voilat L, Devidas A, Morschhauser F, Rohrlich P, André M, Lepage E, Ferme C, SFGM/GELA Study Group (1999) Feasibility of tandem autologous stem-cell transplantation (ASCT) in induction failure or very unfavorable (UF) relapse from Hodgkin's disease (HD). SFGM/GELA study group. Ann Oncol 10:1485–1488
11. Jonkhoff AR, De Kreuk AM, Franschman G et al (2002) Granulocyte colony-stimulating factor mobilized whole blood containing over 0.3 x 106/kg CD34+ cells is a sufficient graft in autologous transplantation for relapsed non-Hodgkin's lymphoma. Br J Haematol 118:90–100
12. Puig N, de la Rubia J, Remigia MJ et al (2009) Morbidity and transplant-related mortality of CBV and BEAM preparative regimens for patients with lymphoid malignancies undergoing autologous stem-cell transplantation. Leuk Lymphoma 47:1488–1494. https://doi.org/10.1038/sj.bmt.1704110
13. Sharma A, Kayal S, Iqbal S, Malik PS, Raina V (2013) Comparison of BEAM vs. LEAM regimen in autologous transplant for lymphoma at AIIMS. Springerplus 2:489. https://doi.org/10.1186/2193-1801-2-489
14. Kim JE, Lee DH, Yoo C, Kim S, Kim SW, Lee JS, Park CJ, Huh J, Suh C (2011) BEAM or BuCyE high-dose chemotherapy followed by autologous stem cell transplantation in non-Hodgkin's lymphoma patients: a single center comparative analysis of efficacy and

toxicity. Leuk Res 35:183–187. https://doi.org/10.1016/j.leukres.2010.07.016

15. Vose JM, Carter S, Burns LJ, Ayala E, Press OW, Moskowitz CH, Stadtmauer EA, Mineshi S, Ambinder R, Fenske T, Horowitz M, Fisher R, Tomblyn M (2013) Phase III randomized study of rituximab/carmustine, etoposide, cytarabine, and melphalan (BEAM) compared with iodine-131 tositumomab/BEAM with autologous hematopoietic cell transplantation for relapsed diffuse large B-cell lymphoma: results from the BMT CTN 0401 trial. J Clin Oncol 31:1662–1668. https://doi.org/10.1200/JCO.2012.45.9453
16. Nieto Y, Popat U, Anderlini P, Valdez B, Andersson B, Liu P, Hosing C, Shpall EJ, Alousi A, Kebriaei P, Qazilbash M, Parmar S, Bashir Q, Shah N, Khouri I, Rondon G, Champlin R, Jones RB (2013) Autologous stem cell transplantation for refractory or poor-risk relapsed Hodgkin's lymphoma: effect of the specific high-dose chemotherapy regimen on outcome. Biol Blood Marrow Transplant 19:410–417. https://doi.org/10.1016/j.bbmt.2012.10.029
17. Caballero MD, Rubio V, Rifon J, Heras I, García-Sanz R, Vázquez L, Vidriales B, Cañizo MC, Corral M, Gonzalez M, León A, Jean-Paul E, Rocha E, Moraleda JM, Miguel JFS (1997) BEAM chemotherapy followed by autologous stem cell support in lymphoma patients: analysis of efficacy, toxicity and prognostic factors. Bone Marrow Transplant 20:451–458. https://doi.org/10.1038/sj.bmt.1700913
18. Bhatia S, Robison LL, Francisco L, Carter A, Liu Y, Grant M, Baker KS, Fung H, Gurney JG, McGlave P, Nademanee A, Ramsay NK, Stein A, Weisdorf DJ, Forman SJ (2005) Late mortality in survivors of autologous hematopoietic-cell transplantation: report from the Bone Marrow Transplant Survivor Study. Blood 105:4215–4222. https://doi.org/10.1182/blood-2005-01-0035