Hematopoietic Progenitor Cell Transplantation in Children, Adolescents, and Young Adults With Relapsed Mature B-Cell NHL

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ABSTRACT

Although children, adolescents, and young adults with newly diagnosed B-cell non-Hodgkin's lymphoma enjoy excellent overall survival with current chemoimmunotherapy, those with relapsed and/or refractory disease have a dismal prognosis. Although most clinicians would agree that hematopoietic progenitor cell transplantation after reinduction therapy is frontline therapy for these patients, there is no consensus as to what type of hematopoietic progenitor cell transplantation promises the best event-free and overall survival. This review outlines the disparate types of stem cell therapy that have been used in this difficult-to-treat population as well as the role of maintenance and CAR T-cell therapy in conjunction with stem cell therapy.

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Children, adolescents, and young adults (CAYAs) with newly diagnosed B-cell non-Hodgkin's lymphoma (B-NHL) enjoy excellent overall survival (OS) with current frontline chemoimmunotherapy.^{1–3} However, those with relapsed and/or refractory (R/R) disease have had a historically dismal OS of $\leq 30\%$ despite reinduction therapy and autologous hematopoietic progenitor cell transplantation (autoHCT) (Figure 1).^{1,2,4–6} Specifically, patients with lactate dehydrogenase ≥ 2 times the upper limit of normal (ULN) at diagnosis, R/R disease within 6 months of diagnosis, multisite relapse, and/or R/R disease with bone marrow involvement experience a significantly decreased OS (Table 1).^{1,7} Consensus guidelines in this difficult-to-treat population are challenging to create given the small numbers of patients and multiple treatment options in this era of burgeoning cellular and immunotherapy. HCT, whether it be autologous, allogeneic, or tandem, has been and continues to be an integral part of therapy, with varying outcomes as delineated in Table 2. This review outlines autologous, allogeneic, tandem HCT; maintenance therapy after stem cell transplantation; and the role of CAR T-cell therapy as it relates to HCT as therapies for R/R B-NHL.

Autologous Transplantation

AutoHCT has historically been considered frontline therapy for CAYAs with R/R B-NHL.^{8,9} Gross et al⁵ conducted a Center for International Blood and Marrow Transplant Research (CIBMTR) retrospective study on CAYAs aged ≤ 18 years with R/R B-NHL who underwent autologous (n=90) or allogeneic (n=92) HCT in 1990 through 2005. The 5-year event-free survival (EFS) rate was similar after autoHCT versus allogeneic HCT (alloHCT) in diffuse large B-cell lymphoma (DLBCL) (52% vs 50%), Burkitt lymphoma (27% vs 31%), and anaplastic large cell lymphoma (35% vs 46%). In the Children's Oncology Group prospective study designed to determine the safety and efficacy of CBV (cyclophosphamide/carmustine/etoposide) conditioning and autologous peripheral blood

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Figure 1. Kaplan-Meier curve showing probability of overall survival in children and adolescents with mature B-cell non-Hodgkin's lymphoma with refractory or relapsed disease during or after therapy in the FAB/LMB96 international study.

From Cairo M, Auperin A, Perkins SL, et al. Overall survival of children and adolescents with mature B cell non-Hodgkin lymphoma who had refractory or relapsed disease during or after treatment with FAB/LMB 96: a report from the FAB/LMB 96 study group. *Br J Haematol* 2018;182:859–869, used with permission from John Wiley & Sons.

HCT in children with R/R Hodgkin lymphoma (HL) and NHL, the 3-year EFS rate from study entry for the 30 patients with NHL was only 30%, whereas the 3-year OS for the 10 patients with NHL who underwent autoHCT was 70%.⁶ Burkhardt et al¹⁰ conducted a retrospective study of CAYAs aged <18 years diagnosed with NHL (excluding anaplastic large cell lymphoma) in or after January 2000 in 24 participating countries who had relapsed or refractory disease. Although survival for the 241 patients who did not undergo HCT was a dismal 9% $\pm$ 2, survival for the 153 patients treated with autoHCT was 55% $\pm$ 5.

Allogeneic Transplantation

AlloHCT is now being used in disparate centers as first-line therapy after salvage therapy for patients with R/R B-NHL.¹¹ Although alloHCT offers the benefit of a graft-versus-lymphoma (GvL) effect, transplant-related mortality and risk of graft-versus-host disease (GVHD) are the weightiest disadvantages to be considered. Many clinicians favor alloHCT for lymphoblastic lymphoma.¹² The aforementioned CIBMTR study revealed a markedly increased 5-year EFS rate of 40% in the patients with lymphoblastic lymphoma who underwent alloHCT compared with 4% in those who underwent autoHCT.⁵ Naik et al¹¹ recently published their institution's experience with allogeneic transplantation for R/R pediatric NHL regardless of subtype in 36 patients, reporting 3-year OS and disease-free survival rates of 67% and 68%, respectively. The 248 patients treated with alloHCT in the Burkhardt et al¹⁰ international

study experienced an OS of 48% $\pm$ 3. The 5-year cumulative incidences of transplant-related mortality and death from disease were 16% $\pm$ 2 and 34% $\pm$ 3, respectively.

Tandem Transplantation

Tandem Autologous

There is adult literature suggesting that tandem autologous transplantation may improve outcomes in patients with R/R HL.^{13–15} There are only 2 studies evaluating tandem autologous transplantation in NHL, both in the adult literature. Although the trial conducted by the GOELAMS group did include patients aged 15 to 60 years, it was an upfront trial in patients with poor-risk NHL; patients with Burkitt's, transformed low-grade, lymphoblastic, or mantle-cell lymphoma were therefore excluded. The study enrolled 45 patients and 31 completed the tandem high-dose therapy autoHCT, with an OS and EFS of 51% and 53%, respectively, and 4 toxic deaths.¹⁶ Hohloch et al¹⁷ conducted a phase II trial of tandem autologous transplantation with interim myeloablative radioimmunotherapy with [¹³¹I]anti-CD20 antibody in 16 adults with R/R lymphoma; 7 were unable to undergo radioimmunotherapy due to toxicity or progressive disease. The 4-year OS and progression-free survival (PFS) rates were 67% and 64%, respectively. Hohloch et al¹⁸ subsequently conducted a prospective multicenter study using modified carmustine/etoposide/cytarabine/melphalan (BEAM) with triple autologous transplantation in adults with R/R NHL. Only 16 of the 24 evaluated patients completed therapy in accordance with the protocol, and 8 had to cease therapy secondary to grade III/IV toxicities. The 1- and 3-year EFS rates for all patients were 38% and 33%, respectively, and the 1- and 3-year OS rates were 50% and 38%, respectively. The trial was terminated early due to toxicity.

Tandem Autologous and Allogeneic

Tandem myeloablative conditioning autoHCT followed by reduced-intensity conditioning (RIC) allogeneic transplantation harnesses the strengths of both autoHCT and alloHCT. AutoHCT provides the benefit of disease eradication with myeloablative therapy. RIC alloHCT provides a GvL effect, with less transplant-related mortality. Carella et al¹⁹ premiered this approach in adult patients with R/R lymphoma. In their cohort of 15 patients (10 HL and 5 NHL), 11 experienced a complete response, 9 of whom had only achieved a partial response after autoHCT. Crocchiolo et al²⁰ reported a 68% 5-year PFS in 34 patients with high-risk relapsed NHL who underwent tandem autoHCT followed by alloHCT at 2 centers in Italy. In a larger retrospective analysis of 111 patients with high-risk

Table 1. Univariate and Multivariate Prognostic Analyses of Survival After Relapse in CAYA NHL Treated With FAB/LMB96 Therapy

	Univariate Analysis			Multivariate Analysis			Multivariate Analysis		
	All Patients (n=67)			All Patients (n=65 ^a)			Burkitt Lymphoma (n=55 ^a)		
	n	5-Year Rate	P Value	HR	95% CI	P Value	HR	95% CI	P Value
LMB89	27	25.9%							
LMB96	23	30.4%							
LMB01	17	35.3%	.60						
Male	50	24.0%							
Female	17	47.1%	.12						
<15 y	56	26.8%							
≥15 y	11	45.5%	.054						
Stage I	2	100%							
Stage II	4	50.0%							
Stage III	33	30.3%							
Stage IV	10	20.0%							
ALL	18	22.2%	.24						
Group A	3	66.7%		1 ^b			1 ^b		
Group B LDH <2 N ^a	12	75.0%							
Group B LDH >2 N ^a	27	14.8%		4.6	1.5–13.8		4.1	1.3–12.4	
Group C	23	17.4%	.005	6.6	2.1–20.6	.005	6.3	2.0–19.9	.007
No DLBCL	57	22.8%		1					
DLBCL	10	70.0%	.003	0.21	0.06–0.70	.012			
Time to relapse ≤6 mo	45	22.2%		1			1		
Time to relapse >6 mo	22	45.5%	.02	0.45	0.21–0.96	.04	0.39	0.18–0.88	.02
Relapse in one site	33	42.4%		1			1		
Multiple site relapse	34	17.7%	.004	3.1	1.6–6.1	.0006	3.3	1.7–6.5	.0005
No CNS relapse	42	33.3%							
CNS relapse	25	24.0%	.33						
No BM relapse	41	39.0%							
BM relapse	26	15.4%	.009						
Salvage chemotherapy									
CYVE	35	40.0%							
Methotrexate	10	10.0%							
ICE	5	60.0%							
Other	15	13.3%	.007						
No rituximab	51	25.5%							
Rituximab	16	43.8%	.29						

Abbreviations: ALL, acute lymphoblastic leukemia; BM, bone marrow; CAYA, childhood, adolescent, and young adult; CNS, central nervous system; CYVE, cytarabine with etoposide; DLBCL, diffuse large B-cell lymphoma; HR, hazard ratio; ICE, ifosfamide/carboplatin/etoposide; LDH, lactate dehydrogenase; N, upper limit of normal; NHL, non-Hodgkin's lymphoma.

^aLDH missing for 2 patients of group B.

^bReference category is patients of group A and group B LDH <2 N.

From Jourdain A, Auperin A, Minard-Colin V, et al. Outcome of and prognostic factors for relapse in children and adolescents with mature B-cell lymphoma and leukemia treated in three consecutive prospective "Lymphomes Malins B" protocols. A Société Française des Cancers de l'Enfant study. *Haematologica* 2015;100:813, with permission.

lymphoma who underwent tandem autoHCT followed by alloHCT, Crocchiolo et al²¹ again proved the safety and efficacy of this approach, reporting that the 39 patients with aggressive NHL and chemosensitive disease obtained a 3-year PFS of 65%. Chen et al²² reported the largest prospective series to date of tandem autoHCT followed by alloHCT in high-risk lymphoma. Among the

42 patients enrolled in their study, 29 (69%) underwent an RIC alloHCT after their myeloablative conditioning autoHCTs. The 2-year PFS and OS rates for patients who underwent tandem HCT were previously unprecedented in this group, at 72% and 89%, respectively. Our group pioneered this approach in CAYAs with R/R lymphoma in a prospective study using myeloablative

Table 2. HCT in Children, Adolescents, and Young Adults With Relapsed/Refractory NHL

Author	Center/ Group	N	Age (y)	NHL Histology	Donor Source	Conditioning Regimen	DFS/EFS (%)
Philip et al, 1988 ⁴⁷	SFOP	15	NA	B-NHL	14 auto 1 allo	BEAM/BEAC Other	27
Loiseau et al, 1991 ⁴⁸	Institut Gustave Roussy	24	NA	16 B-NHL 8 T-NHL	Auto	BU/CY BU/Melphalan	33
Bureo et al, 1995 ⁴⁹	Spain	46	1–17	21 LL 19 B-NHL 6 LCL	14 allo 32 auto	BEAM CY/TBI CY/TBI/Ara-C	58
Ladenstein et al, 1997 ⁵⁰	EBMT	89	2.8–16.2	B-NHL	Auto	BACT 31 BEAM 23 BU/CY 9 Other 26	44 (sensitive relapse)
Fanin et al, 1999 ⁵¹	EBMT	64	3.2–53	ALCL	Auto	N/A	47
Kobrinisky et al, 2001 ⁵²	CCG	50	<21	N/A	Auto	N/A	50
Levine et al, 2003 ⁵³	CIBMTR	128	2–67	LL	Auto	N/A	39
Woessmann et al, 2006 ⁵⁴	BFM	20	1–15.8	ALCL	Allo	TBI/CY/VP-16	75
Won et al, 2006 ⁵⁵	Korea	33 76	1.7–16 5–53	6 B-NHL 13 LL 14 LCL	Auto Allo	BEAM BEAC CBV TBI regimen N/A	59 36
Gross et al, 2010 ⁵	CIBMTR	90 92		52 DLBCL 53 LL 41 BL 36 ALCL	90 auto 92 allo	NA	DLBCL 52 (auto) 50 (allo) BL 27 (auto) 31 (allo) ALCL 35 (auto) 46 (allo) LL 4 (auto) 40 (allo)
Harris et al, 2011 ⁶	COG	10	4.2–19.9	NA	Auto	CBV	70
Giulino-Roth et al, 2013 ⁵⁶	MSKCC (US)	21 15	3.5–20.9	12 LL 5 BL 4 DLBCL 13 ALCL 1 PTCL 1 u-NHL	21 allo 15 auto	CY/TBI CY/THIO/TBI TBI/other Non-TBI-based	53
Jourdain et al, 2015 ⁷	SFOP	33 8	NA	NA	8 allo 33 auto	BEAM, BAM, BU/MEL, TBI/CY, other	49 (auto) 38 (allo)
Satwani et al, 2015 ²³	Multicenter US trial	10	7–33	3 ALCL 2 DLBCL 3 BL 1 LL 1 PTCL	Tandem Auto Allo	BEC (auto) BU/FLU ± rATG (allo)	70
Burkhardt et al, 2018 ¹⁰	International trial	153 248	0.3–18	152 BL 101 T-LL Remaining 148: DLBCL + PMBL + B-LL + other	153 auto 248 allo	NA	55 (auto) 47 (allo)

(continued on next page)

Table 2. HCT in Children, Adolescents, and Young Adults With Relapsed/Refractory NHL (cont.)

Author	Center/ Group	N	Age (y)	NHL Histology	Donor Source	Conditioning Regimen	DFS/EFS (%)
Gardenswartz et al, 2018 ²⁴	Multicenter US trial	13	7–33	8 BL 3 DLBCL 2 PMBL	Tandem Auto Allo	BEC (auto) BU/FLU ± rATG (allo 12) BEAM (allo 1)	91
Naik et al, 2019 ¹¹	TCH	36	4–24	14 ALCL 8 T-LL 1 B-LL 8 DLBCL 1 BL 1 small cell, non-Burkitt high-grade lymphoma 1 T-cell-rich, B-cell lymphoma 1 stem cell myeloproliferative/T-cell lymphoma 1 hepatosplenic γδ T-cell lymphoma	Allo	MAC 27 RIC 9	68

Abbreviations: ALCL, anaplastic large cell lymphoma; allo, allogeneic; Ara-c, cytarabine; B-LL, B-lymphoblastic lymphoma; BEAC, carmustine/etoposide/Ara-C/cyclophosphamide; auto, autologous; BACT, bischloroethylnitrosourea/cytarabine/cyclophosphamide/6-thioguanine; BAM, busulfan/cytarabine/melphalan; BEAM, carmustine/etoposide/cytarabine/melphalan; BEC, carmustine/etoposide/cyclophosphamide; BFM, Berlin-Frankfurt-Münster; BL, Burkitt lymphoma; B-NHL, B-cell non-Hodgkin's lymphoma; BU, busulfan; CBV, cyclophosphamide/carmustine/etoposide (VP-16); CCG, Children's Cancer Group; COG, Children's Oncology Group; CY, cyclophosphamide; CIBMTR, Center for International Bone Marrow Transplant Registry; DFS, disease-free survival; DLBCL, diffuse large B-cell lymphoma; EBMT, European Society for Blood and Marrow Transplantation; EFS, event-free survival; FLU, fludarabine; HCT, hematopoietic progenitor cell transplantation; LCL, large cell lymphoma; LL, lymphoblastic lymphoma; MAC, myeloablative conditioning; MEL, melphalan; MSKCC, Memorial Sloan Kettering Cancer Center; N, number; NA, not available; N/A, not applicable; NHL, non-Hodgkin's lymphoma; PMBL, primary mediastinal B-cell lymphoma; PTCL, peripheral T-cell lymphoma; rATG, rabbit antithymocyte globulin; RIC, reduced-intensity conditioning; SFOP, Société Française d'Oncologie Pédiatrique; TBI, total body irradiation; TCH, Texas Children's Hospital; T-LL, T-lymphoblastic lymphoma; T-NHL, T-cell non-Hodgkin's lymphoma; THIO, thiotepa; u-NHL, undifferentiated NHL; VP-16, etoposide.

Modified from Bradley MB, Cairo MS. Stem cell transplantation for pediatric lymphoma: past, present and future. *Bone Marrow Transplant* 2008;41:150; with permission.

conditioning autoHCT with subsequent RIC alloHCT,²³ reporting an overall 10-year EFS of 50% in an intent-to-treat analysis of all enrolled patients with HL versus a 70% EFS in patients who received a tandem myeloablative conditioning autoHCT and RIC alloHCT. We have reported a 91% EFS in a cohort of 13 CAYA patients with R/R B-NHL (5 of whom were part of our original cohort) who underwent myeloablative conditioning autoHCT with subsequent radioimmunotherapy with yttrium-90-ibritumomab tiuxetan followed by RIC alloHCT with a median follow-up of 48 months.²⁴ There were no reports of myelodysplastic syndromes or secondary leukemias and no transplant-related mortality in this cohort to date.

Maintenance After HCT

In this era of targeted, immune, and cellular therapy, there is a paradigm in patients with HL for a maintenance therapy regimen post HCT that offers promising results. The AETHERA trial revealed an almost 20% increase in PFS in patients with unfavorable-risk relapsed or primary refractory HL randomized to receive brentuximab vedotin (BV) post autoHCT compared with those who were randomized to the placebo arm.²⁵ An expert panel comprising members of the American Society for Blood

and Marrow Transplantation (now called American Society for Transplantation and Cellular Therapy), CIBMTR, and the European Society for Blood and Marrow Transplantation (EBMT) that recently convened to create consensus statements regarding maintenance therapies for HL and NHL endorsed BV maintenance and/or consolidation in BV-naïve high-risk HL.²⁶ In a recent case study, Flerlage et al²⁷ described their retrospective review of 5 pediatric patients with R/R HL who received BV post autoHCT. All 5 patients were reported to be alive and in CR with a 29- to 76-month follow-up time from initiation of consolidation. The Collaborative Trial in Relapsed Aggressive Lymphoma randomized 242 patients post BEAM conditioning and autoHCT to either rituximab maintenance (every 2 months for 1 year) or observation and reported no difference in 4-year EFS or OS between the 2 arms.²⁸ Rituximab maintenance did yield an increased 10-year PFS in the phase III EBMT study that randomized patients with relapsed follicular lymphoma to either maintenance rituximab or observation (54% vs 37%). This statistically significant PFS did not translate into a difference in OS.²⁹ Rituximab maintenance therapy also proved efficacious for mantle cell lymphoma in a phase III study that randomized 240 patients to rituximab

maintenance or observation post R-BEAM autoHCT. Patients in the rituximab maintenance arm experienced a 4-year EFS, PFS, and OS of 79%, 83%, and 89%, respectively, compared with 61%, 64%, and 80% in the observation arm ($P=.001$).³⁰ Myriad agents are being evaluated currently as maintenance therapies post autoHCT in adults with B-NHL, including ibrutinib, bortezomib, lenalidomide, and pembrolizumab. In their evaluation of ways to improve outcomes of autologous transplantations in lymphoma, Dahi et al¹³ deem maintenance therapy as having the most promise in attaining that goal.

Polatuzumab Maintenance After HCT

Polatuzumab vedotin (PV), an antibody–drug conjugate that targets CD79b antigens on the surface of human B cells and that is linked to monomethyl auristatin E (MMAE), a potent tubulin inhibitor, is a promising candidate for maintenance therapy in patients with B-NHL post HCT. Palanca-Wessels et al³¹ demonstrated that PV had an acceptable safety and tolerability profile in 68 patients with NHL. In addition, they went on to demonstrate an objective response in 23 of 42 evaluable patients given single-agent PV (specifically 14 of 25 with DLBCL) and 7 of 9 patients treated with PV and rituximab. A series of subsequent phase II studies used PV in combination with other chemotherapy agents, including in combination with rituximab, in patients with R/R DLBCL. Of the 39 patients enrolled in the rituximab plus PV arm in the ROMULUS study, 54% had an objective response, whereas 21% had a CR.³² Sehn et al³³ recently published their findings in patients aged >18 years with transplant-ineligible R/R DLBCL treated with either PV plus bendamustine and rituximab (BR) versus PV plus bendamustine and obinutuzumab. The phase II 1:1 randomization comparing PV BR versus BR showed that CR rates were significantly higher (40% vs 17.5%) and risk of death was reduced by 58% in the PV BR group. PV was also studied up-front in newly diagnosed DLBCL in combination with chemotherapy.³⁴ PV is generally well tolerated. The most common grade 3–4 events reported in the single-agent study by Palanca-Wessels et al³¹ were neutropenia, anemia, and peripheral sensory neuropathy.

CAR T-Cell Therapy Before and After HCT

CAR T-cell therapy is changing the landscape of R/R NHL therapy. There are now 2 FDA-approved CARs for adult B-NHL.^{35,36} CARs are artificial receptors composed of an antigen-specific, monoclonal antibody–derived single-chain variable fragment bound to an intracellular signaling domain. Specifically directed CARs incorporated into T cells or natural killer cells create an opportunity for

target-specific recognition to be combined with cellular activation. Potential advantages of CAR-based immunotherapy over monoclonal antibody therapy include diffuse biodistribution, stimulation of the adaptive immune system, and sustained immune activity (or a so-called living drug).^{37,38} Although 4-1BB CARs persist for a longer amount of time, CD28 CARs have faster and more robust expansion.^{39,40} Tisagenlecleucel and axicabtagene ciloleucel (axi-cel) are the 2 currently FDA-approved CAR therapies for DLBCL. Axi-cel is also FDA-approved for primary mediastinal B-cell lymphoma.³⁵ Tisagenlecleucel is an anti-CD19 second-generation CAR with a 4-1BB costimulatory domain. In the phase II JULIET trial, 40% of the 93 adults who underwent infusion had a CR and 12% a partial response (PR); 12 months after initial response, relapse-free survival was 65%.⁴¹ Axicabtagene ciloleucel is an anti-CD19 second-generation CAR with a CD28 costimulatory domain. In the phase II ZUMA trial, 54% of the 101 patients who underwent infusion experienced a CR and 28% a PR.⁴² There are no currently FDA-approved CARs for pediatric NHL. Rivers et al⁴³ presented 8 pediatric patients receiving CAR-T therapy as 1:1 ratio of CD4 and CD8 cells for DLBCL, primary mediastinal B-cell lymphoma, Burkitt lymphoma, and gray zone lymphoma. Only 3 of 8 patients experienced a CR, whereas 5 of 8 experienced a CR or PR; however, the CRs were not sustained. The NIH currently has an anti-CD22 CAR T-cell therapy trial open for pediatric patients with recurrent/refractory CD22-expressing B-cell malignancies (ClinicalTrials.gov identifier: NCT02315612).

In a pooled analysis of published CD19 CAR T-cell therapy in patients with B acute lymphoblastic leukemia, Taraseviciute et al⁴⁴ note that a greater number of relapses occurred in patients who did not proceed to HCT after CAR T-cell therapy. Although CAR T-cell therapy can be used as a bridge to transplant, the CAR T-cells are then eradicated with pretransplant conditioning. Providing CAR T-cells in conjunction with alloHCT is an appealing prospect because they can immediately provide a GvL effect and serve as bridging therapy until immune reconstitution post HCT occurs and the GvL from the allograft takes effect, although there is some concern that immunosuppression post alloHCT might affect the efficacy of CAR T-cells.⁴⁴ Kochenderfer et al⁴⁵ treated 10 patients with CD19-positive NHL post alloHCT whose disease did not respond to standard-donor lymphocyte infusions with donor-derived CD19 CAR-T cells. Two patients with chronic lymphocytic leukemia achieved a CR and 1 patient with mantle cell lymphoma achieved a PR; none of the 10 patients developed GVHD. Kochenderfer's group⁴⁶ went on to treat 20 patients with CD19-positive NHL post alloHCT with donor-derived

CD19 CAR-T cells; 6 achieved a CR and 2 a PR. Not one of the 20 patients developed GVHD.

Conclusions

In this thrilling age of rapidly evolving cellular and immune therapy, there is a cornucopia of therapeutic combinations to choose from in CAYAs with R/R B-NHL. Given the small group of patients who experience disease relapse, it is difficult to design randomized controlled trials to compare all of these options. Despite the promising response rates to CD19 CAR T-cell therapy in adults with R/R B-NHL, there are limited data in CAYAs at this point and neither of the 2 FDA-approved CARs are indicated for Burkitt lymphoma, the most common subtype of pediatric B-NHL. Our standard approach includes reinduction therapy, and for those experiencing a PR/CR we proceed with myeloablative conditioning and autoHCT, including yttrium-90-ibritumomab tiuxetan in the myeloablative conditioning,

followed by an RIC alloHCT as we have previously described.²⁴

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