Special Article

Hematopoietic Stem Cell Transplantation for Patients with Advanced-Stage Follicular Lymphoma

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Patients with advanced-stage follicular lymphoma (FL) are considered to be incurable and eventually relapse after conventional chemotherapy. High-dose therapy (HDT) followed by autologous hematopoietic stem cell transplantation (AHSCT) can unequivocally prolong the disease-free survival (DFS) but not overall survival (OS) in the first complete remission and in a salvage setting. Recently, the incorporation of rituximab and radioimmunoconjugates in HDT with AHSCT seems to be promising and widely accepted. Although allogeneic hematopoietic stem cell transplantation (alloHSCT) consistently demonstrates longer DFS compared with historical controls of HDT followed by AHSCT, this approach cannot be considered as a standard of care due to its unacceptably high treatment-related mortality (TRM) and the lack of improving OS. With highly encouraging results and less TRM, the role of nonmyeloablative hematopoietic stem cell transplantation (NMHSCT), especially after AHSCT, needs to be validated in randomized controlled trials with a long-term follow-up.

Keywords: *Follicular lymphoma, Autologous hematopoietic stem cell transplantation, Allogeneic hematopoietic stem cell transplantation, Nonmyeloablative hematopoietic stem cell transplantation*

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Follicular lymphoma (FL) is characterized by long-term survival (median survival, 8-12 years). At diagnosis, the majority of patients are relatively asymptomatic, and only a small number of them present with early-stage disease. Despite being with advanced-stage disease, many patients still have long-term survival without initial therapy[1-3]. Because of the nature of this disease, most of the patients are incurable by conventional chemotherapy. This review focuses on the most recent developments of the role of autologous hematopoietic stem cell transplantation (AHSCT) and allogeneic hematopoietic stem cell transplantation (alloHSCT) for patients either with newly diagnosed or relapsed and refractory advanced-stage FL.

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AHSCT as salvage therapy

A number of phase II trials have demonstrated that high-dose chemoradiotherapy followed by AHSCT for relapsed or refractory advanced-stage FL can improve disease-free survival (DFS) (Table 1)[4-10]. A long-term follow-up study reported by Rohatiner et al has suggested that prolonged freedom from recurrence in patients with FL treated in second or subsequent remission with AHSCT is plateau on the survival curve after 12 years[8]. In addition, the same study has demonstrated that both remission duration and overall survival (OS) time of patients underwent AHSCT in second remission were significantly longer than that of patients treated with standard chemotherapy regimens ($p < 0.0001$ and $p = 0.02$, respectively)[8].

A three-arm prospective randomized trial (CUP trial) was compared between conventional salvage therapy (C), AHSCT using unpurged autografts (U),

Table 1. Autologous stem cell transplantation for follicular lymphoma in relapsed disease

Study	n	Preparative regimen	*Ex vivo* purging	Stem cell source	Median F/U (years)	DFS/PFS	OS	Early TRM	Incidence of tMDS/AML	Comments
Bierman et al[4]	100	Cy/TBI or BEAM	None	BM 13%, PB 87%	2.6	44% at 4 years	65% at 4 years	8%	2%	-
Freedman et al[5]	153	Cy/TBI	Anti-B mAb + C'	BM 100%	8.0	42% at 8 years	66% at 8 years	<1%	7.8%	-
Apostolidis et al[6]	99	Cy/TBI	Anti-B mAb + C'	BM 100%	5.5	63% at 5.5 years	69% at 5.5 years	4%	12%	-
Van Besien et al[7]	131	TBI 34%, non-TBI 66%	mAb 11%, CD34+ selection 21%, chemotherapy 68%	BM 76%, PB 24%	4.1	39% at 5 years	62% at 5 years	8%	5%	14% TRM at 5 years
Van Besien et al[7]	597	TBI 31%, non-TBI 69%	None	BM 15%, PB 85%	3.4	31% at 5 years	55% at 5 years	4%	9%	8% TRM at 5 years
Rohatiner et al[8]	121	Cy/TBI	Anti-B mAb + C'	BM 100%	13.5	55% at 5 years 48% at 10 years	71% at 5 years 54% at 10 years	3%	12.4%	-
Schouten et al[9]	32	Cy/TBI	Anti-B mAb	BM 100%	5.8	55% at 2 years	77% at 4 years	6.3%	NS	RCT
Schouten et al[9]	33	Cy/TBI	None	BM 100%	5.8	58% at 2 years	71% at 4 years	9%	NS	RCT
Hosing et al[10]	68	Cy/VP-16/ TBI 99%, BEAM 1%	Anti-CD19 mAb 82%	BM 85%, PB 9%, Both 6%	5.9	17% at 8.3 years	34% at 8.3 years	6%	6%	-

F/U = follow up; DFS = disease-free survival; PFS = progression-free survival; OS = overall survival; TRM = treatment-related mortality, early TRM usually defined as occurring within 100 days after transplantation; tMDS/AML = transplant-related myelodysplastic syndrome/acute myeloid leukemia; Cy = cyclophosphamide; TBI = total body irradiation; BEAM = BCNU/etoposide/cytarabine/melphalan; BM = bone marrow; PB = peripheral blood; mAb = monoclonal antibody; C' = complement; NS = not specified; RCT = randomized controlled trial

and AHSCT using purged autografts (P) as consolidation therapy following successful re-induction therapy in patients with recurrent advanced-stage FL[9]. Unfortunately, only 89 patients were randomly assigned at the end of the study. Although the study showed a significantly improved progressive-free survival (PFS) and (OS) in favor of both AHSCT arms, it is still inconclusive due to the small number of patients enrolled in the study and the imbalances of risk factors in the third patient subgroups.

AHSCT in first complete remission

As part of consolidation for patients with advanced-stage FL in first complete remission, high-dose therapy (HDT) followed by AHSCT is based on the efficacy of such an approach in heavily pretreated and relapsed patients. Recently, three prospective randomized trials have confirmed the benefit of AHSCT in terms of prolonged PFS but not OS (Table 2)[11-13].

A multicenter randomized controlled trial by GOELAMS (Groupe Ouest-Est des Leucemies et Autres Maladies du Sang)[11] randomly assigned 172 patients with newly diagnosed advanced-stage FL to receive either an immunochemotherapy regimen (cyclophosphamide, doxorubicin, teniposide, prednisone, and interferon) or a HDT followed by purged AHSCT. As compared with the patients who received chemotherapy and interferon, those treated with HDT had a significantly higher complete response rate and very good partial response rate (55% vs. 81%, p = 0.045). According to the intention-to-treat analysis, the event-free survival (EFS) at 5 years differed significantly between the reference chemotherapy and HDT groups (48% vs. 60%, p = 0.05); the 5-year OS did not differ significantly between groups (84% vs. 78%, p = 0.49).

The German Low-Grade Lymphoma Study Group (GLSG)[12] conducted a multicenter randomized controlled trial to compare the effect of potentially curative myeloablative radiochemotherapy followed by AHSCT with interferon-alpha (IFN-alpha) maintenance therapy in 307 young patients (aged 18-59) with advanced-stage FL in their first complete remission after two cycles of cyclophosphamide-doxorubicin-vincristine-prednisone (CHOP) or mitoxantrone-chlorambucil-prednisone (MCP) induction chemotherapy. Two hundred and forty patients were evaluable for the comparison of AHSCT and IFN-alpha. Five-year PFS for patients treated with HDT followed by AHSCT was significantly higher than that of patients treated with IFN-alpha (64.7% vs. 33.3%, p < 0.0001). However, longer follow-up is necessary to determine the effect

Table 2. Autologous stem cell transplantation for follicular lymphoma in first complete remission

Study	n	Preparative regimen	*Ex vivo* purging	Stem cell source	Median F/U (years)	DFS/PFS	OS	Early TRM	Incidence of tMDS/AML	Comments
Deconick et al[11]	86	TBI/Cy	CD34+ selection 75%, immunomagnetic purging 13%, none 12%	BM 16%, PB 84%	5.0	60% at 5 years	78% at 5 years	0%	7%	RCT and intention to treat analysis
Lenz et al[12, 18]	140	TBI/Cy	None	PB 100%	4.1	62% at 5 years	NS	1%	6.6%	RCT and intention to treat analysis
Sebban et al[13]	192	Cy/VP-16/TBI	None	PB 100%	7.7	40% at 7 years	71% at 7 years	<1%	1%	RCT

F/U = follow up; DFS = disease-free survival; PFS = progression-free survival; OS = overall survival; TRM = treatment-related mortality, early TRM usually defined as occurring within 100 days after transplantation; tMDS/AML = transplant-related myelodysplastic syndrome/acute myeloid leukemia; TBI = total body irradiation; Cy = cyclophosphamide; BM = bone marrow; PB = peripheral blood; RCT = randomized controlled trial; NS = not specified; VP-16 = etoposide

of AHSCT on OS. As predicted, treatment related mortality (TRM) was higher in the AHSCT group, but early mortality was below 2.5% in both study arms.

The Groupe d'Etude des Lymphomes de l'Adulte[13] conducted a multicenter randomized controlled trial (GELF94) to compare six monthly courses of cyclophosphamide-doxorubicin-teniposide-prednisone (CHVP) followed by 6 bimonthly courses combined with IFN-alpha-2b 5 million units three times weekly for 18 months to four courses of CHOP followed by cyclophosphamide/etoposide/total body irradiation (TBI) and AHSCT in young patients (aged 18-60) with newly diagnosed FL and a high tumor burden. Two hundred nine patients were randomized into the chemotherapy arm and 192 into the transplantation arm. Pretreatment clinical and biological characteristics were equally distributed in two treatment groups. The overall response in transplantation arm was similar to that in the chemotherapy arm (78% vs. 79%, p = NS). With a median follow-up of 92 months, 7-year EFS estimate for transplantation arm was longer than that for the chemotherapy arm but did not meet statistically significant level (38% vs. 28%, p = 0.11). An estimated 7-year OS for the transplantation arm was similar to the chemotherapy arm (76% vs. 71%, p = 0.53). After the central pathology review, 339 of the 401 patients enrolled in this trial were confirmedly diagnosed as FL. For those 339 patients, 7-year EFS was better in the patients who underwent transplantation than those who underwent only chemotherapy (40% vs. 29%, p = 0.05); however, OS was equal (p = 0.4). Fourteen cases of secondary malignancies including four cases of treatment-related myelodysplastic syndrome and acute leukemia (t-MDS/AML) were reported in the chemotherapy arm, whereas 11 cases of secondary malignancies were reported in the transplantation arm including two cases of t-MDS/AML.

Graft purging

Tumor-cell contamination of autograft is thought to be a major risk that contributes to relapse after AHSCT in patients with FL. Pre-AHSCT purging may reduce the rate of relapse.

***Ex vivo* purging vs. unpurging graft**

This issue has not yet been well addressed by both phase II and recently phase III trials. Results from phase II trials including Dana-Faber group[5], Standford group[14], and IBMTR/ABMTR[7] suggest an advantage of purging autograft in terms of improving PFS and OS; whereas the English group[6] does not. Unfortunately, all recent phase III trials do not evaluate the benefit of purging autograft[11-13].

***In vivo* vs. *ex vivo* purging**

Van Heeckeren et al[15] have conducted a study to compare the feasibility, safety, and efficacy of *in vivo* purging with rituximab and *ex vivo* purging with CliniMACS CD34 cell enrichment device in patients with CD20+ non-Hodgkin's lymphoma (NHL) receiving AHSCT. Twenty-seven patients were randomized to either *in vivo* purging with rituximab or *ex vivo* purging by CD34+ cell selection. The elimination of B-cells in autograft was equally efficient in both methods. When compared with an *in vivo* purging, an *ex vivo* purging was associated with CD34+ cell loss and delayed median neutrophil (10 days vs. 11 days) and platelet (12.5 days vs. 17 days) count recoveries. Lymphocyte recovery was similar in both methods, whereas immunoglobulin recovery was delayed after *in vivo* purging. At a median follow-up of 27 months, 2-year probability of EFS for *in vivo* purging and *ex vivo* purging was 81% and 76%, respectively (p = 0.66). When compared with 53 unpurged patients, all 27 purged patients had significantly improved 3-year probability of OS (89% vs. 70%, p = 0.014) and a trend for improved EFS (78% vs. 57%, p = 0.075)[15].

T-MDS/AML after AHSCT

A major concern of AHSCT is the risk of inducing t-MDS/AML which was varied from 1-12% in several retrospective studies including heavily pretreated patients[8,16,17] and varied from 1-7% in previously mentioned 3 prospective randomized studies[11,13,18]. The correlation of the conditioning regimens and the risk of developing t-MDS/AML have failed to demonstrate by recent studies[18,19]. Based on a subgroup analysis of GLSG, the authors suggested that the type of pretransplantation chemotherapy regimens, not the conditioning procedure per se, did have impact on the risk of t-MDS/AML, which was 5.1% at 5 years after MCP (mitoxantrone, chlorambucil and predisolone) and only 1% after CHOP[18]. At a median follow-up of three years, a group from City of Hope Comprehensive Cancer Center reported an association between VP-16-primed stem cell mobilization, not the pretransplantation chemotherapy or conditioning regimens, and a 12.3-fold increased risk of developing t-AML with 11q23/21q22 abnormalities (p = 0.006) in patients with NHL and HL underwent high-dose chemoradiotherapy and AHSCT[19].

AlloHSCT

Conventional myeloablative alloHSCT has been used as a consolidation therapy for patients with recurrent FL, which contributed to a graft-versus-lymphoma effect (GVL) and circumvented the tumor cell contamination associated with AHSCT. Even though there has not been phase III trial performed, several phase II trials have consistently shown a lower risk of relapse compared with AHSCT. However, they do not translate to improving OS since the significantly increased risk of TRM associated with alloHSCT has offset the survival benefit (Table 3)[7,10,20]. A group from M.D. Anderson Cancer Center has performed a retrospective analysis on patients with chemoresistant FL undergone myeloablative alloHSCT that demonstrated a long-term DFS and plateaus of either DFS or OS at 24 and 44 months, respectively[10].

Nonmyeloablative hematopoietic stem cell transplantation (NMHSCT)

Although NMHSCT for patients with FL provides a less TRM, an incidence of GVHD is still a major cause of death in these patients (Table 4)[21-24]. The study from M.D. Anderson Cancer Center[21], evaluated 20 patients with relapsed indolent NHL including 18 patients with FL. All patients received salvage therapy followed by NMHSCT with a conditioning regimen consisting of fludarabine, cyclophosphamide with or without rituximab. After transplantation, all patients achieved CR with both DFS and OS of 84%. The TRM was 10%, whereas the incidence of grade II to IV acute graft-versus-host disease (GVHD) and chronic GVHD was 20% and 64%, respectively. Recently, a Japanese study[22] has reported 45 heavily pretreated patients with indolent NHL including 14 patients with chemoresistant tumors. These patients received a fludarabine or low-dose total body irradiation (TBI)-based regimen followed by NMHSCT. The 3-year PFS for chemosensitive and chemoresistant patients was 83% and 64%, respectively. The TRM was 18%, whereas the grade II to IV acute GVHD and chronic GVHD was 49% and 59%, respectively. Although the TRM in patients underwent NMHSCT is lower than that of whom underwent conventional myeloablative alloHSCT, GVHD remains a major cause of mortality[7,20-22]. Two different English multicenter studies[23,24], which incorporated anti-CD52 monoclonal antibody into the conditioning-regimen to eliminate *in vivo* donor T cells, demonstrated the lower incidence of acute and chronic GVHD compared with previously mentioned studies without an increased incidence of graft rejection[21-24]. In addition, such an approach has demonstrated the benefit of NMHCT in patients with relapsed and refractory FL in terms of improving DFS and OS.

AHSCT vs. alloHSCT

To date, there is no available randomized controlled trial to compare the outcome of AHSCT and alloHSCT among patients with recurrent or refractory advanced-stage FL. Hosing et al conducted a retrospective study to compare the outcome of 44 patients who underwent myeloablative alloHSCT from match-sibling donor with 68 patients who underwent AHSCT[10]. The characteristics of patients in both groups were similar with respect to age at transplantation, gender, histological subtypes, number of chemotherapy regimens received before transplantation, and International Prognostic Index scores (IPI). However, patients in the AHSCT group significantly had more chemosensitive diseases, more complete response at the time of transplantation, and longer median time from diagnosis to transplantation than those in the alloHSCT group. In the alloHSCT group, the median follow-up time was 53 months (range 21-113), and the OS and DFS were 49% and 45%, respectively. In the AHSCT group with a median follow up time of 71 months (range 22-109) after treatment, the OS and DFS were 34% and 17%, respectively. Outcomes were initially more favorable for the AHSCT group (significant only for day 100 mortality); however, this pattern changed over time. A plateau was seen among the alloHSCT group at 44 months after transplantation for OS and at 24 months for DFS, whereas there was a continuous pattern of treatment failure in the AHSCT group. The improved DFS was significant ($p = 0.01$) among the alloHSCT group but was not translated to the significant improvement of OS ($p > 0.05$). However, a similar pattern of DFS was observed when 19 patients with chemoresistant disease who underwent alloHSCT were compared with 26 patients with chemosensitive disease who underwent AHSCT ($p = 0.04$). The rate of disease progression was significantly higher in the AHSCT group than that in the alloHSCT group (74% vs. 19%, $p = 0.003$).

Prospective

An antibody-based therapy, both unconjugated antibodies and radioimmunconjugates, seems to have promising antilymphoma activity in patients with recurrent FL. Early studies have suggested that an *ex vivo* purging of autograft to eradicate contaminating

Table 3. Allogeneic stem cell transplantation for follicular lymphoma

Study	n	Preparative regimen	Stem cell source	Median F/U (years)	DFS/PFS	OS	Early TRM	Relapse	Incidence of tMDS/AML	Comments
Van Besien et al[7]	176	TBI 68%, non-TBI 32%	BM 77%, PB 23%	3	45% at 5 years	51% at 5 years	24%	21% at 5 years	0%	20% GVHD
Hosing et al[10]	44	Cy/VP-16/TBI 55%, BEAM 45%	BM 41%, PB 59%	4.4	45% at 10 years	49% at 10 years	34%	19% at 1.2 years	0%	No relapse after 430 days of transplant, 55% acute GVHD, 45% chronic GVHD
Peniket et al[20]	231	Varied regimens	NS	5	43% at 4 years	51% at 4 years	NS	25% at 4 years	NS	Case matched study, 38% TRM at 4 years

F/U = follow up; DFS = disease-free survival; PFS = progression-free survival; OS = overall survival; TRM = treatment-related mortality, early TRM usually defined as occurring within 100 days after transplantation; tMDS/AML = transplant-related myelodysplastic syndrome/acute myeloid leukemia; TBI = total body irradiation; BM = bone marrow; PB = peripheral blood; GVHD = graft-versus-host disease; NS = not specified; Cy = cyclophosphamide; VP-16 = etoposide; BEAM = BCNU/etoposide/cytarabine/melphalan

Table 4. Nonmyeloablative stem cell transplantation for follicular lymphoma

Study	n	Preparative regimen	Stem cell source	Median F/U (years)	DFS/PFS	OS	Early TRM	Relapse	Incidence of tMDS/AML	Comments
Khouri et al[21]	20	Flud/TBI	PB 100%	1.75	84% at 2 years	84% at 2 years	5%	NS	NS	20% cumulative acute GVHD, 64% cumulative chronic GVHD
Kusumi et al[22]	44	Flud based regimens or TBI or others	BM 80%, PB 20%	2	83% at 2 years	79% at 2 years	NS	NS	NS	9% TRM-associated with GVHD
Faulkner et al[23]	28	BEAM/Campath	PB 100%	1.3	69% at 2 years	74% at 2 years	16%	20% at 2 years	NS	No extensive chronic GVHD
Morris et al[24]	41	Campath/Flud Melphalan	NS	3	65% at 3 years	73% at 3 years	2%	44% at 3 years	NS	Low incidence of grade III/IV GVHD

F/U = follow up; DFS = disease-free survival; PFS = progression-free survival; OS = overall survival; TRM = treatment-related mortality, early TRM usually defined as occurring within 100 days after transplantation; tMDS/AML = transplant-related myelodysplastic syndrome/acute myeloid leukemia; Flud = fludarabine; TBI = total body irradiation; PB = peripheral blood; NS = not specified; GVHD = graft-versus-host disease; BM = bone marrow; BEAM = BCNU/etoposide/cytarabine/melphalan

lymphoma cells might be associated with prolonged DFS[25]. In order to reduce the number of contaminating lymphoma cells by an *in vivo* purging, recent studies have included the rituximab into the preparative regimen before AHSCT or after AHSCT as consolidation to get rid of residual disease. Two pilot studies reported the feasibility and safety of immunochemotherapy consisting of an *in vivo* purging with rituximab followed by AHSCT in patients with relapsed or refractory FL[26,27]. Another two small single-institution studies were conducted to evaluate the efficacy of *in vivo* purging with rituximab followed by AHSCT. Galimberti et al[28] conducted a study on 23 patients with FL who received either high-dose chemotherapy alone (n = 12) or in combination with rituximab (11 patients) after induction therapy with CHOP. Patients in the combination group achieved a polymerase chain reaction (PCR)-negative harvest in 86% compared with only 14% in the high-dose chemotherapy alone group. All patients re-infused with negative aphereses achieved CR and showed a better but not significant 5-year PFS compared to those reinfused with contaminated samples (100% vs. 41%, p = 0.15). Belhadj et al[29] designed a sequential treatment with rituximab, then a mobilization chemotherapeutic regimen and followed by HDT with peripheral blood stem cell transplantation for patients with relapsed follicular, marginal zone and mantle cell lymphomas (11, 2, and 1 case, respectively). PCR analyses were performed in peripheral blood before rituximab, during follow-up, and at harvest. Nine of the 11 studied cases (82%) were free of PCR-detectable molecular marker in harvests. After HDT, clinical complete remission (cCR) and molecular remission were achieved in 13 (93%) patients and in 11 (79%) patients, respectively. With a median follow-up of 3 years, the 14 transplanted patients were alive, 11 of them remaining in cCR and eight in molecular remission at last follow-up[29].

Another appealing approach is to substitute for the unselective TBI a targeted radiation therapy by applying radioimmunoconjugates in a myeloablative dose followed by AHSCT[30]. The feasibility of ^{131}I-labeled antibody tositumomab myeloablative radioimmunotherapy (RIT) has been successfully demonstrated in 125 patients with refractory or relapsed FL[30]. The patients enrolled in the study were treated either with myeloablative RIT (n = 27) or with conventional, mostly TBI-based, myeloablative radiochemotherapy (n = 98) followed by AHSCT. After a single myeloablative infusion of 131-I-tositumomab, 23 (85%) of 27 patients achieved a complete remission/complete remission unconfirmed (CR/CRu) and an overall response (CR/CRu and partial remission) of 93%. The estimated 5-year OS and PFS in patients treated with myeloablative dose-RIT were 67% and 48%, respectively compared with only 53% and 29% in those treated with conventional AHSCT[30]. Notably, the risk for t-MDS/AML did not differ between the two treatment groups.

Another concept is the combination of RIT such as ^{90}Y-labeled ibritumomab tiuxetan or the ^{131}I-labeled tositumomab and high-dose chemotherapy. The feasibility and the safety of a phase I/II trial of high-dose ^{90}Y-labeled ibritumomab tiuxetan in combination with high-dose etoposide and cyclophosphamide followed by AHSCT have been demonstrated in eight patients with poor-risk or relapsed FL[31]. At the median follow-up of 22 months (range 2-44 months), the 2-year os and relapse-free survival (RFS) were both 100%. In a phase I/II study, 34 (65.3%) of 52 patients with grade I/II FL were treated with high-dose ^{131}I-labeled tositumomab followed by etoposide and cyclophosphamide and AHSCT. For all patients, the 2-year estimated OS and PFS were 83% and 68%, respectively, which were favorably comparable to previous results in a historical control group treated with TBI, etoposide, and cyclophosphamide[32]. In order to enhance the feasibility and safety of this approach, a conventional dose of ^{131}I-labeled tositumomab was combined with standard BEAM (BCNU [carmustine], etoposide, cytarabine, and melphalan) and followed by AHSCT. This treatment seemed to be well tolerated with non-significant additional toxicity compared with historical controls treated with BEAM alone[33].

Conclusion

Recently, several prospective randomized controlled trials have consistently demonstrated that AHSCT after myeloablative therapy can significantly prolong the DFS in patients with advanced-stage FL in first CR and in salvage setting. However, this approach cannot be recommended as the consolidation therapy after first CR because of no improvement of OS and possible tMDS/AML. The best explanation for an ineffective improvement of OS is a contamination of lymphoma cells in an autograft, which may be eliminated by an incorporation of anti-CD20 monoclonal antibody into the HDT followed by AHSCT. The role of rituximab and RIT in this approach is necessary to be further investigated in prospective trials.

Although patients underwent myeloablative alloHSCT have significantly less relapse and disease

progression compared with AHSCT and conventional therapy, this approach cannot be considered as a standard of care due to its unacceptably high TRM and the lack of improving OS. With highly encouraging results and less TRM, the role of NMHSCT in patients with recurrent or relapsed FL, especially after AHSCT, needs to be validated in randomized controlled trials with long-term follow-up.

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การปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดในผู้ป่วยมะเร็งต่อมน้ำเหลืองชนิด follicular lymphoma ระยะลุกลาม

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การรักษาผู้ป่วยมะเร็งต่อมน้ำเหลืองชนิด follicular lymphoma (FL) ระยะลุกลามด้วยเคมีบำบัดขนาดมาตรฐาน ไม่สามารถทำให้ผู้ป่วยหายขาดจากมะเร็งได้ การรักษาด้วยเคมีบำบัดขนาดสูงตามด้วยการปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดของผู้ป่วยเอง (autologous hematopoietic stem cell transplantation) สามารถเพิ่มระยะเวลาที่ผู้ป่วยปลอดจากโรค แต่ยังคงไม่สามารถเพิ่มระยะเวลาการอยู่รอดของผู้ป่วยได้ ไม่นานมานี้การรักษาผู้ป่วยมะเร็งต่อมน้ำเหลืองกลุ่มนี้ด้วย rituximab และ radioimmunoconjugates หลังจากที่ผู้ป่วยได้รับเคมีบำบัดขนาดสูง ตามด้วยการปลูกถ่ายไขกระดูกของผู้ป่วยเองแล้ว พบว่าได้ผลดีและเป็นที่ยอมรับมากขึ้น ถึงแม้ว่าการรักษาด้วยเคมีบำบัดขนาดสูงตามด้วยการปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดจากผู้บริจาค (allogeneic hematopoietic stem cell transplantation) จะเพิ่มระยะเวลาการปลอดจากโรคมากกว่าการปลูกถ่ายเซลล์ต้นกำเนิด เม็ดเลือดจากตัวผู้ป่วยเองก็ตาม การรักษาดังกล่าวยังไม่ถือว่าเป็นการรักษามาตรฐาน เนื่องจากการรักษาด้วยวิธีนี้มีผลข้างเคียงมาก และไม่สามารถขยายระยะเวลาการอยู่รอดของผู้ป่วยกลุ่มนี้ได้จริง สำหรับการรักษาด้วยการปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดจากผู้บริจาคชนิดไม่ทำลายไขกระดูกอย่างถาวร (nonmyeloablative hematopoietic stem cell transplantation) โดยเฉพาะอย่างยิ่งในผู้ป่วยที่เคยได้รับการรักษาด้วยเคมีบำบัดขนาดสูงตามด้วยการปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดของผู้ป่วยเองมาก่อนพบว่าได้ผลดี แต่ยังคงต้องทำการศึกษาเพิ่มเติมและติดตามผลการรักษาในระยะยาวต่อไป