

High-Dose Therapy and Autologous Hematopoietic-Cell Transplantation for Follicular Lymphoma Beyond First Remission: The Stanford University Experience

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Received July 7, 2000; accepted March 22, 2001

ABSTRACT

A retrospective analysis was performed to investigate the outcome of high-dose therapy (HDT) and autologous hematopoietic cell transplantation in patients with follicular lymphomas beyond first remission. Ninety-two patients with primary induction failure or relapsed follicular low-grade lymphoma (FLGL), follicular large cell lymphoma (FLCL), and transformed follicular lymphoma (TFL) were treated with myeloablative therapy consisting of etoposide (60 mg/kg), cyclophosphamide (100 mg/kg), and either carmustine (BCNU; 15 mg/kg) or fractionated total body irradiation (FTBI; 1200 cGy) followed by transplantation of purged autologous bone marrow or peripheral blood hematopoietic cells. For the 49 patients with relapsed FLGL, the median age was 49 years and the median interval from diagnosis to HDT was 30 months. The 4-year estimate of overall survival (OS) was 60% (95% confidence interval [CI], 45%-75%) and of disease-free survival (DFS) was 44% (95% CI, 29%-59%). Treatment with the FTBI-containing HDT regimen was associated with significantly longer DFS ($P = .04$) and OS ($P = .04$) in our multivariate analysis. OS was also significantly longer among those treated with 3 or fewer chemotherapy regimens. For the 26 FLCL patients, the median age was 51 years and in 31% the indication for HDT was primary induction failure. For FLCL patients, the 4-year estimate of OS was 58% (95% CI, 37%-79%) and of DFS was 51% (95% CI, 30%-72%). Among the 17 patients with TFL, 13 (76%) transformed at first relapse, and only 6 patients (35%) achieved complete remission with salvage therapy prior to HDT. For TFL patients, the 4-year estimate of OS was 50% (95% CI, 24%-76%) and of DFS 49% (95% CI, 20%-78%). There were 3 occurrences of myelodysplasia (1 after treatment with TBI, 2 after BCNU treatment), yielding an estimated incidence of 7% (95% CI, 0%-16%) at 56 months. This analysis shows that relapsed FLGL patients treated with 3 or fewer different chemotherapy regimens show inferior survival. The HDT regimen containing FTBI appears to be superior to the BCNU-based regimen for relapsed FLGL, although longer follow-up is needed to evaluate late effects. Lastly, patients with TFL or induction failure and relapsed FLCL can achieve survival outcome comparable to those observed with the indolent follicular lymphomas.

KEY WORDS

Follicular lymphoma • High-dose therapy • Autologous hematopoietic cell transplantation

INTRODUCTION

The role of high-dose therapy (HDT) with autologous hematopoietic cell transplantation for patients with relapsed follicular low-grade lymphoma (FLGL) has been examined by a number of studies [1-9]. Although these studies have yielded considerable information regarding survival outcome, few consistent prognostic variables that correlate with

outcome have been identified, and whether there is an optimal preparative regimen has not been established.

In this study we describe the results of our single-institution 10-year experience with HDT and purged autologous hematopoietic cell transplantation in 92 patients with follicular lymphoma who were not in first remission. Within this group were 49 patients with relapsed FLGL. We have

Table 1. Histologic Subgroups for All Patients

	No. of Patients
Follicular low-grade lymphoma	49
Follicular small	15
Follicular mixed	22
Mixed architecture follicular small	3
Mixed architecture follicular mixed	9
Follicular large cell lymphoma	26
Follicular large	14
Mixed architecture follicular large	12
Transformed follicular lymphoma	17
From follicular small/mixed	12
From follicular large	5
Total	92

also analyzed outcome for 26 patients with induction failure or relapsed follicular large cell lymphoma (FLCL) and 17 patients with transformed follicular lymphoma (TFL). Our aim was to investigate outcome and to identify potential prognostic factors.

PATIENTS AND METHODS

Patients

A computerized database query was used to identify 94 consecutive patients treated with HDT who were registered with a histologic diagnosis of follicular lymphoma. This number did not include FLGL patients in first remission treated with HDT under a separate research protocol that concurrently accrued patients during the active study period. In addition, excluded from this analysis were 2 patients who had discordant lymphomas with synchronous diffuse large cell lymphoma at distant sites. A retrospective review of the clinical data was performed for the remaining 92 patients. All patients were treated with HDT and autologous hematopoietic cell transplantation between March 9, 1988, and March 24, 1999. The median follow-up among all surviving patients for the entire group at the time of this analysis was 56 months (range, 8-134 months). The initial diagnostic biopsy specimens from all patients were available for review and the histologic characteristics are summarized in Table 1. Forty-nine patients were categorized as having FLGL following a diagnosis of follicular small cleaved cell or follicular mixed NHL as defined by the International Working Formulation [10]. Patients with a mixed architectural pattern were also considered to have FLGL if the cell type was small cleaved cell or mixed small cleaved and large cell and any follicular component was present. Twenty-six patients were classified as having FLCL as previously described [11]. Seventeen patients had histologically proven TFL; in 12 of these patients, the disease had undergone conversion from FLGL to a diffuse large cell lymphoma. Five additional patients with an original diagnosis of FLCL transformed to diffuse large cell lymphoma were included in this analysis as TFL.

All patients were treated following written informed consent under a research protocol approved by the Stanford University Medical Center Administrative Panel on Medical Human Subjects. Inclusion criteria required relapsed disease following attainment of remission with conventional therapy, failure to achieve a complete remission following initial

therapy, or progressive disease during initial therapy. Although strict definitions of minimal disease status were not implemented, demonstration of sensitivity to chemotherapy prior to HDT was required for all patients. Exclusion criteria included abnormal hepatic function, prior hematopoietic cell transplantation procedures, and severe psychological disorders or serious comorbid conditions.

Collection and Processing of Hematopoietic Cells

Bone marrow was harvested from the posterior iliac crests while the patient was under general anesthesia [12]. Peripheral blood hematopoietic cells were collected via apheresis following "mobilization" with cyclophosphamide 4 gm/m², and granulocyte colony-stimulating factor (G-CSF; 10mg/kg per day with the dose rounded to the nearest vial size). With the exception of the first 3, for all patients the autograft was density fractionated on a Percoll gradient and "purged" with monoclonal antibodies and rabbit complement prior to cryopreservation as previously described [13]. A panel of monoclonal antibodies directed against B lymphocytes was used and included J9 (anti-CD9), 4-35 (anti-CD10), J149 (anti-CD19), and 1F5 (anti-CD20) (Chromaprobe Inc, Mountain View, CA).

High-Dose Therapy and Autologous Hematopoietic Cell Transplantation

Patients were treated with a myeloablative HDT regimen consisting of fractionated total body irradiation (FTBI) in 10 equal fractions to a total dose of 1200 cGy, etoposide 60 mg/kg, and cyclophosphamide 100 mg/kg as previously described [14]. Carmustine (BCNU) at a dose of 15 mg/kg, to a maximum of 550 mg/m², was substituted for FTBI if the patient had received prior radiotherapy to the chest or pelvis, if excessive morbidity with FTBI was anticipated on the basis of higher age (over 60 years) or poor Karnofsky's performance status (<70%), or if patients refused to undergo total body irradiation [14]. During the initial period of accrual, patients were received transplants of monoclonal antibody-purged autologous bone marrow (n = 36). Subsequent to September 29, 1993, all patients (n = 56) received autologous peripheral blood hematopoietic cells with the exception of 2 patients who failed to "mobilize" adequately with chemotherapy and G-CSF and thus received transplants of "purged" autologous bone marrow [15]. Posttransplantation supportive care was delivered according to standard institutional practice as previously described [14].

Statistical Analysis

Outcome was analyzed with respect to overall survival (OS) and disease-free survival (DFS). OS time was defined as time from HDT to death from any cause or until last follow-up evaluation for patients who were alive. DFS was defined as time from HDT to relapse or progression of disease from best remission, death from any cause, or until last follow-up if none of these events had occurred. For the entire patient group and the subset of patients with FLGL, Cox proportional hazards univariate and multivariate regression models for both categorical and continuous variables were used to identify predictors of OS and DFS [16]. Significance ($P \leq .05$) was determined from the Wald χ^2 test. The Kaplan-Meier method was used to estimate the actuarial OS and DFS, and

Table 2. Patient Characteristics*

	FLGL (n = 49)	FLCL (n = 26)	TFL (n = 17)
Age, median (range), y	48 (32-59)	51 (32-66)	47 (28-68)
Male/female, n	29/20	18/8	9/8
Stage at diagnosis, n			
I/II	5	6	5
III	11	9	3
IV	33	11	9
B symptoms, n	6	2	2
Bulky mass (>10 cm), n	4	4	4
Extranodal disease, n			
Marrow	34	13	8
Extramedullary	22	6	4
Diagnosis to HDT, median (range), mo	30 (9-178)	21.5 (7-301)	37 (8-152)

*n indicates number of patients; FLGL, follicular low-grade lymphoma; FLCL, follicular large cell lymphoma; TFL, transformed follicular lymphoma; HDT, high-dose therapy.

differences between the patient groups were assessed with the log-rank test [17,18]. Differences in the median observations and proportions of patient characteristic variables between the groups treated with the FTBI and the non-FTBI regimen were determined with the Wilcoxon rank sum test and the Fisher exact test, respectively [19].

RESULTS

Patient Characteristics

The patient characteristics for the 49 patients with FLGL, the 26 patients with FLCL, and the 17 patients with TFL are summarized in Table 2. The median age at the time of HDT for the group as a whole was 48 years (range, 28-68 years). The median time from diagnosis to HDT for the group as a whole was 30 months (range, 7-301 months). At initial diagnosis most patients with FLGL had stage IV disease, 22 of whom (45%) had nonmarrow extranodal involvement that included skin (n = 4), central nervous system (n = 2), gastrointestinal tract (n = 6), and pleural fluid (n = 4) at some point prior to HDT. Only a few patients from all 3 groups had either B symptoms or a bulky mass prior to HDT.

For the 17 TFL patients, transformation was histologically documented at first relapse in 13 (76%), and at second relapse in the remaining 4 patients. At the time of transformation, 10 patients (59%) had stage IV disease. The median time interval from diagnosis to histologic transformation was 35 months (range, 7-149 months). The median interval from transformation to HDT was 3 months (range, 2-20 months).

Treatment Prior to High-Dose Therapy

The characteristics and response to initial therapy prior to HDT for all patients are summarized in Table 3. All patients had been previously treated with chemotherapy prior to consideration for HDT. Twelve (24%) FLGL, 4 (15%) FLCL, and 4 (24%) TFL patients had been treated with 3 or more different chemotherapy regimens prior to HDT. With the exception of 3 FLGL patients who received fludarabine and 2 TFL patients who had been treated with rituximab, all

patients received chemotherapy courses of alkylator-based multiple-agent regimens. Forty-one FLGL patients (84%) received combination chemotherapy as part of their initial therapy; 19 of the 41 received cyclophosphamide, vincristine, and prednisone and the remainder received various doxorubicin-based regimens. The median time interval from diagnosis to initiation of therapy was 4 months (range, 1-110 months) for FLGL patients. Twenty-five FLCL patients (96%) received induction chemotherapy; the majority of them (81%) received standard doxorubicin-containing combination chemotherapy. Eighteen FLCL patients (70%), compared with 29 FLGL patients (59%), achieved a first complete remission following initial therapy. Median times to progression following initial therapy for patients with FLGL and FLCL were 7.5 months and 11.5 months, respectively.

Approximately 1 of 5 patients had also received radiotherapy prior to HDT. Eighteen patients received irradiation as part of initial therapy, which included central nervous system prophylaxis for 2 patients with TFL and local/regional field irradiation in the remainder. Three FLGL patients and 1 FLCL patient received irradiation alone as initial therapy.

At the time of histologic transformation, salvage therapy for the 17 TFL patients was as follows: 14 patients were treated with combination chemotherapy, 2 received radiotherapy alone, and 1 received rituximab. The response for these patients included 6 (35%) complete remissions and 11 (65%) partial remissions.

Patient Characteristics at High-Dose Therapy

Characteristics of HDT and outcome are summarized in Table 4. Twenty FLGL patients (41%) had histologic evidence of marrow involvement by lymphoma at the time of HDT; the median marrow involvement by lymphoma was

Table 3. Characteristics of Pre-HDT Therapy and Response for All Patients*

	FLGL (n = 49)	FLCL (n = 26)	TFL (n = 17)
Number of chemotherapy regimens, n			
1	8	7	2
2	29	15	11
≥3	12	4	4
Number of chemotherapy cycles, n			
1-6	8	6	2
7-12	26	12	9
>12	15	6	6
Radiotherapy, n	10	6	6
Response to initial therapy, n			
Complete remission	29	18	11
Partial remission	18	0	5
Progressive disease or primary induction failure	2	8	0
Time to progression following initial therapy, median (range), mo	7.5 (1-72)	11.5 (3-207)	13.2 (1-108)

*n indicates number of patients; HDT, high-dose therapy; FLGL, follicular low-grade lymphoma; FLCL, follicular large cell lymphoma; TFL, transformed follicular lymphoma.

Table 4. HDT Characteristics and Outcome for All Patients*

	FLGL (n = 49)	FLCL (n = 26)	TFL (n = 17)
Marrow involvement at HDT, n	20	2	2
Disease status at HDT, n			
First PR or primary induction failure	1	8	0
Second PR	32	9	7
Second CR	9	6	6
≥3 PR/CR	7	3	4
HDT regimen, n			
FTBI/VP/CY	38	14	8
BCNU/VP/CY	11	12	9
Graft, n			
Bone marrow	19	10	7
Peripheral Blood	30	16	10
MoAb-purged	48/49	24/26	17/17
OS 4-y estimate (95% CI), %	60 (45-75)	58 (37-79)	50 (24-76)
DFS 4-y estimate (95% CI), %	44 (29-59)	51 (30-72)	49 (20-78)

*n indicates number of patients; HDT, high-dose therapy; FLGL, follicular low-grade lymphoma; FLCL, follicular large cell lymphoma; TFL, transformed follicular lymphoma; PR, partial remission; CR, complete remission; FTBI, fractionated total body irradiation; VP, etoposide; CY, cyclophosphamide; BCNU, carmustine; MoAb, monoclonal antibody; OS, overall survival; CI, confidence interval; DFS, disease-free survival.

5% (range, 5%-15%). Most FLGL patients were given HDT in second partial remission, although 9 patients (18%) were in second complete remission at the time of HDT. Eight FLCL patients (31%) underwent HDT with primary induction failure as the indication. As noted above, 6 TFL patients (35%) achieved a second complete remission after histologic transformation and received HDT with that disease status, with most of the remainder in second partial remission.

Thirty-eight FLGL and 14 FLCL patients were treated with the FTBI-containing regimen, and the remainder received BCNU in conjunction with etoposide and cyclo-

Table 5. Patient Characteristics According to HDT Regimen for FLGL Patients*

	FTBI (n = 38)	Non-FTBI (n = 11)	P Value
Age, median (range), y	46 (32-59)	54 (40-58)	.01†
Stage IV at diagnosis, n	27	6	.16
Pre-HDT treatment, n			
≥3 Chemotherapy regimens	10	2	.28
Radiotherapy	6	4	.11
HDT disease status, n			
First PR or primary induction failure	0	1	NA
Second PR/CR	33	8	.27
≥3 PR/CR	5	2	.32

*n indicates number of patients; HDT, high-dose therapy; FLGL, follicular low-grade lymphoma; FTBI, fractionated total body irradiation; PR, partial remission; NA, not assessed; CR, complete remission.

†Difference between FTBI and non-FTBI groups statistically significant ($P \leq .05$).

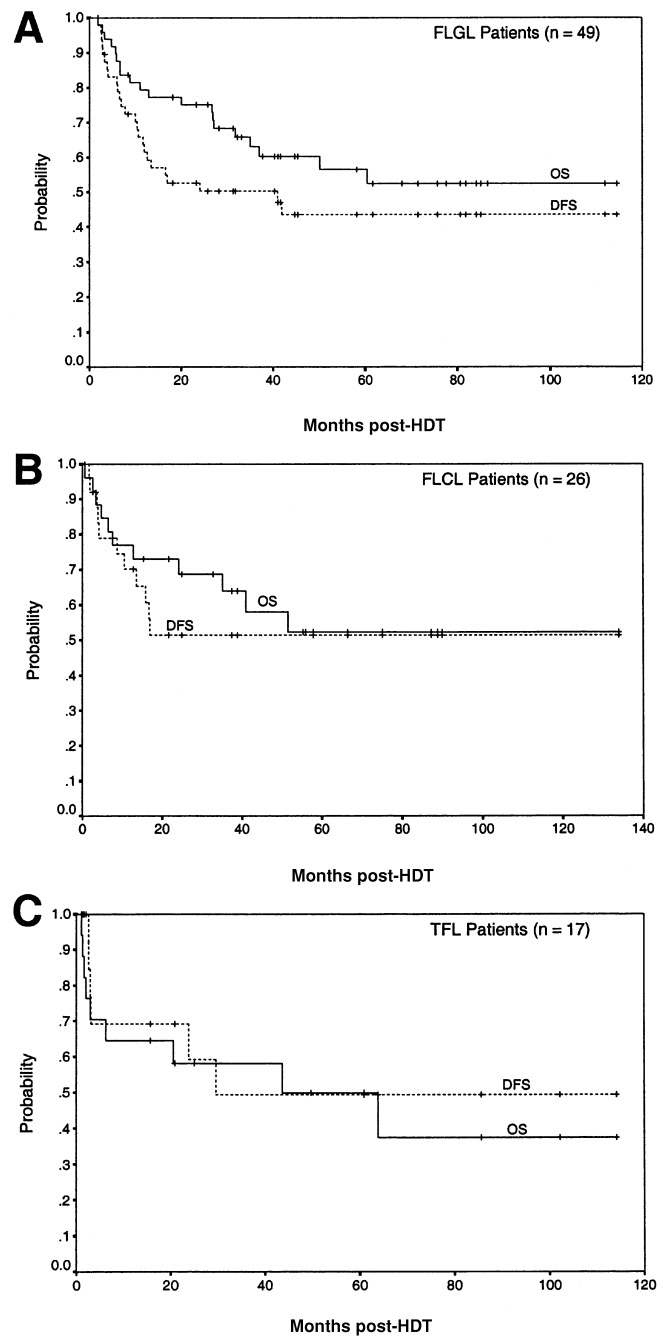


Figure 1. Overall survival (OS) and disease-free survival (DFS) for patients with (A) follicular low-grade lymphoma (FLGL), (B) follicular large cell lymphoma (FLCL), and (C) transformed follicular lymphoma (TFL).

phosphamide. Patient characteristics according to the HDT regimen for FLGL patients are summarized in Table 5. The median age for FLGL patients treated with FTBI was significantly lower, an expected finding given the selection criteria used for determining HDT regimen.

Treatment Outcome

There were 9 deaths (10%) during the early posttransplantation period prior to day 120. Four patients died of

Table 6. Univariate Analysis for Entire Patient Group and for FLGL Subset*

Factor	P Values for All Patients (n = 92)		P Values for FLGL Patients (n = 49)		Favorable
	OS	DFS	OS	DFS	
Age	.47	.58	.16	.72	
Histology (low grade versus all patients)	.70	.78	NA	NA	
Stage (I-III vs. IV)	.17	.21	.46	.88	
B symptom	.75	.92	.53	.49	
Bulky mass	.96	.92	.65	.74	
Extranodal disease (marrow)	.26	.36	.73	.77	
Initial therapy: no. of regimens (1-2 vs. ≥ 3)	.003†	.22	.001†	.06	With <3 different regimens
Initial therapy: response (CR vs. non-CR)	.80	.47	.77	.45	
Initial therapy: time to progression	.40	.41	.08	.23	
Disease status at HDT					
(CR vs non-CR)	.80	.32	.82	.89	
(<3 vs. ≥ 3 PR/CR)	.54	.79	.06	.11	
Marrow involvement at HDT					
HDT regimen (FTBI vs. non-FTBI)	.04†	.04†	.001†	.06	With FTBI-containing regimen
Graft (marrow vs. peripheral blood)	.28	.50	.26	.09	

*The Cox proportional hazards regression model was used to generate *P* values for both continuous and categorical variables as determined by the Wald χ^2 test, with OS and DFS measured from the time of HDT. FLGL indicates follicular low-grade lymphoma; OS, overall survival; DFS, disease-free survival; CR, complete remission; HDT, high-dose therapy; PR, partial remission; FTBI, fractionated total body irradiation.

†Statistically significant ($P \leq .05$).

diffuse alveolar hemorrhage, 2 of hepatic veno-occlusive disease, 2 of aspergillus infection, and 1 of gastrointestinal bleeding due to a gastric arterio-venous malformation at day 103 post-HDT. Two additional patients experienced late deaths while in continued remission, one at day 385 with multi-organ failure, and the other at day 956 from bacterial sepsis.

Three patients developed secondary myelodysplasia during the period before follow-up at 28, 30 and 64 months after HDT. Two had received the BCNU-containing HDT regimen. The estimated actuarial incidence for this complication was 7% at 56 months (95% CI, 0%-16%). A complex karyotype was documented in 1 patient, which included deletions of chromosomes 5 and 13. All 3 have died, 2 without evidence of recurrent lymphoma. There were no observed occurrences of secondary epithelial malignancies.

For the remaining 44 FLGL patients who did not experience nonrelapse mortalities or secondary myelodysplasia there have been 25 relapses. Twenty-one patients have remained alive and are in continuous remission; for these patients the median follow-up was 45 months (range, 8-115 months). Eleven relapses were observed for the remaining 22 FLCL patients, whereas 11 patients are alive and, with the median follow-up of 66 months (range, 22-134 months), are in continuous remission. For the 12 remaining TFL patients there were 5 relapses, and 7 patients are alive and in continuous remission with the median follow-up for these patients of 64 months (range, 16-114 months).

The FLGL patients have a Kaplan-Meier estimate at 4 years for OS of 60% (95% CI, 45%-75%) and DFS of 44% (95% CI, 29%-59%). The FLCL patients have a 4-year estimate for OS of 58% (95% CI, 37%-79%), and a DFS of 51% (95% CI, 30%-72%). The TFL patients have a 4-year estimate for OS of 50% (95% CI, 24%-76%), and a DFS of 49% (95% CI, 20%-78%). Kaplan-Meier curves of estimated survival for each group are shown in Figure 1.

Prognostic Models

Univariate analysis of potential prognostic variables by Cox proportional hazards regression for the entire patient group and the subset of FLGL patients is summarized in Table 6. This analysis was not performed for the FLCL and TFL groups because of the small sample size. The same factors were significant correlates of OS and/or DFS for both the entire patient group and the FLGL subset. For FLGL patients, OS was significantly longer for patients who had received fewer than 3 different chemotherapy regimens ($P = .003$) and who were given the FTBI-containing HDT regimen ($P = .04$). The FTBI HDT regimen also significantly correlated with an improved DFS ($P = .04$) for FLGL patients. Kaplan-Meier curves of OS and/or DFS rates for

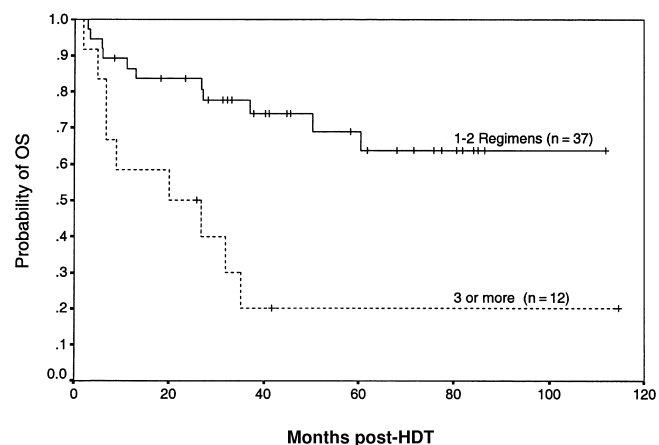


Figure 2. Overall survival (OS) for patients with follicular low-grade lymphoma according to the number of pre-HDT chemotherapy regimens (log-rank $P = .001$).

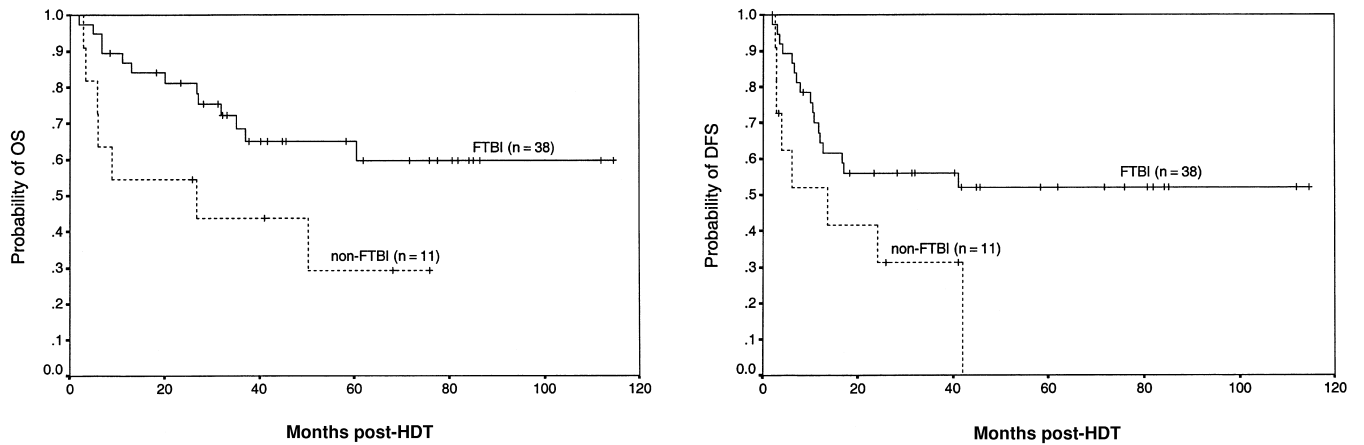


Figure 3. Overall survival (OS) and disease-free survival (DFS) for patients with low-grade follicular lymphoma according to high-dose therapy regimen (log-rank $P = .04$ for OS, and $P = .04$ for DFS).

FLGL patients stratified by pre-HDT chemotherapy regimen number and HDT regimen are shown in Figures 2 and 3, respectively. A trend toward better DFS rates with absence of marrow involvement at the time of HDT ($P = .06$) was observed for FLGL patients but were not significant by univariate analysis. Results of Cox proportional hazards multivariate regression analysis for FTBI-containing HDT regimen, positive marrow at HDT, and number of pre-HDT chemotherapy regimens for FLGL patients with respect to both OS and DFS are summarized in Table 7. All variables significant by univariate analysis maintained significance by multivariate analysis.

The reason for a superior OS rate without an improved DFS rate for FLGL patients who had received fewer than 3 different chemotherapy regimens prior to HDT is not clear. However, it was observed that during the first year following HDT there were 5 deaths (42%) for the group who had been exposed to 3 or fewer chemotherapy regimens; 4 patients of this group died due to early relapse. This number is in contrast to 6 deaths (16%) among those pretreated with fewer than 3 different regimens.

DISCUSSION

We report results with HDT and autologous transplantation for relapsed FLGL that are consistent with the current body of published data. Less heavily pretreated patients with

relapsed FLGL and those who received the FTBI-containing HDT regimen survived longer. We also report results with HDT for 26 patients with FLCL and 17 patients with TFL, adding to the limited outcome data for these patients. The Nebraska group reported on 62 FLCL patients treated with HDT, where an estimated OS rate of 58% was observed at 5 years for those with good prognostic features [20]. Two other groups have reviewed their experience with TFL and had reported survival outcome similar to ours [21,22].

With the expanding number of effective treatment options for patients with relapsed FLGL, their management requires a balance of efficacy and treatment-related toxicity. Fludarabine, targeted immunotherapy with a chimeric anti-CD20 monoclonal antibody, and anti-CD20 radio-immunoconjugates have all produced meaningful responses [23-26]. Novel strategies derived from advances in basic research such as *bcl-2* antisense oligonucleotides and idiotype vaccination may become important alternatives in the future [27,28]. Additionally, the advent of reduced-intensity conditioning for nonmyeloablative allogeneic hematopoietic cell transplantation has renewed interest in inducing a graft-versus-lymphoma effect for these patients, for whom the mortality rates with conventional allogeneic transplantation can be prohibitive [29,30].

Although HDT and autologous transplantation for relapsed FLGL have had consistent reports of durable remissions in a proportion of patients, late effects including

Table 7. Multivariate Analysis for FLGL Patients (n = 49)*

	P Values		RR		Favorable
	OS	DFS	OS (95% CI)	DFS (95% CI)	
Initial therapy: no. of regimens (1-2 vs. ≥3)	.002†	.28	—	4.4 (1.8-11.2)	With <3 different regimens
Marrow involvement at HDT	.6	.01†	—	3.1 (1.3-7.6)	Without marrow involvement
HDT regimen (FTBI vs. non-FTBI)	.02†	.01†	3.7 (1.5-9.7)	3.0 (1.2-7.7)	With FTBI-containing regimen

*Univariately significant factors were analyzed by the Cox proportional hazards regression using a forward stepwise selection method. FLGL indicates follicular low-grade lymphoma; RR, relative risk; OS, overall survival; DFS, disease-free survival; CI, confidence interval; HDT, high-dose therapy; FTBI, fractionated total body irradiation.

†Statistically significant ($P \leq .05$).

secondary myelodysplasia may erode the benefit achieved by disease control [1-9,31]. Recent studies from 2 large centers reported an actuarial incidence for secondary myelodysplasia that approached 20% at 10 years following HDT [32,33]. In most of these cases, the HDT regimen contained FTBI [34,35]. In other reports, the association with FTBI has been questioned and the risk of secondary myelodysplasia was primarily related to therapy received prior to HDT [36-40].

We report both improved OS rates and DFS rates for relapsed FLGL patients treated with FTBI in the HDT regimen, although the patient numbers were small and selection factors were used in regimen assignment. Molina et al. similarly observed superior survival outcome for a FTBI-based HDT regimen in their series of 58 patients with low-grade follicular lymphoma [8]. Our actuarial estimate of secondary myelodysplasia was 7% at 56 months, with 2 of 31 patients treated in the BCNU group developing secondary myelodysplasia compared with 1 of 59 patients treated with FTBI.

Relapse remains the major cause of treatment failure following HDT. Several investigators have reported improved relapse-free survival for FLGL patients who received transplants of purged autografts, particular those rescued with a product that was negative for the t(14;18) rearrangement, by the polymerase chain reaction (PCR) [1,41]. Almost all patients (90 of 92 patients) in this study received transplants of ex vivo "purged" hematopoietic cells from either peripheral blood or bone marrow. Incomplete PCR data for the current patient group precludes similar comparison.

The role and timing of HDT and autologous transplantation must be considered in the context of the patient's remission status and available alternative therapies, several of which are currently the subject of active investigation.

ACKNOWLEDGMENTS

The authors are indebted to the nurses, housestaff, fellows, nurse practitioners, social workers, and case managers of the Stanford University Medical Center for their excellent care of our patients. The authors also thank the technologists of the Stanford University Bone Marrow Transplantation Clinical Laboratory for their competent processing of the autografts. Special mention is made of the Bone Marrow Transplantation data managers who have carefully worked to document and maintain a meticulous record of the care rendered to these patients.

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