Autologous Bone Marrow Transplantation for Acute Myelocytic Leukemia in First Remission: A European Survey of the Role of Marrow Purging


We analyzed data from 263 patients with acute myelocytic leukemia (AML) autografted in first remission (CR) during the period from January, 1982 to January, 1987 at one of 34 centers in the European Bone Marrow Transplant Group. The median age of patients was 30 years (range, 1 to 65). The median interval between achieving CR and autografting was 5 months (range, 1 to 23). Of the 263 patients, 131 patients received cytoreductive regimens that included total body irradiation (TBI); the remainder received various combinations of cytotoxic drugs. Sixty-nine patients received autologous marrow purged in vitro with mafosfamide, and 194 received unpurged marrow. The median follow-up was 28 months (range, 12 to 97). For patients with standard risk AML in CR autografted after TBI (n = 107), the leukemia-free survival (LFS) was higher, and the probability of relapse was lower in recipients of purged than of unpurged marrow (63% versus 34%, P = .05 and 23% versus 55%, relative risk 0.34, P = .006, respectively). The superior results of purging were most obvious in patients autografted within 6 months of achieving CR (probability of relapse, 20% versus 61%, P = .01). Patients with longer intervals between CR and autografting had higher LFS and lower probability of relapse than those autografted early in CR (intervals greater than 9 months, 7 to 9 months, 4 to 7 months, and ≤ 3 months: LFS = 56%, 40%, 35%, 27%, P = .007, probability of relapse = 25%, 56%, 59%, 67%, P = .005; respectively). We conclude that marrow purging with mafosfamide may be valuable for patients autografted early in first CR.

© 1990 by The American Society of Hematology.
Marrow purging in autografting for AML

Table 1. Pre-Autografting Regimens Used in Patients With AML

<table>
<thead>
<tr>
<th>Regimen Description</th>
<th>Patients Treated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CY + TBI; X + TBI CY 60 mg/kg × 2 + TBI 10 Gy</td>
<td>156 (58)</td>
</tr>
<tr>
<td>CY + FTBI; X + FTBI CY 80 mg/kg × 2 + FTBI 10 Gy</td>
<td>32 (12)</td>
</tr>
<tr>
<td>BAVC BCNU 800 mg/m² × 1, AMSA 150 mg/m² × 3, VP16 150 mg/m² × 3, Ara-C 300 mg/m² × 3</td>
<td>26 (10)</td>
</tr>
<tr>
<td>UCH CY 1.5 g/m² × 3, BCNU 300 mg/m² × 1, Ara-C 200 mg/m² × 4, 6TG 200 mg/m² × 4, ADR 50 mg/m² × 1</td>
<td>14 (5)</td>
</tr>
<tr>
<td>BU + Cy Busulfan 4 mg/kg × 4 + CY 50 mg/kg × 4</td>
<td>19 (7)</td>
</tr>
<tr>
<td>HDM Melphalan 140 mg/m²</td>
<td>20 (8)</td>
</tr>
<tr>
<td>Others</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: UCH, Regimen of the University College Hospital (London, UK); HDM, high-dose melphalan; X, additional drug(s).

or at a level reported to be adjusted to the individual sensitivity of granulocyte/macrophage colony forming units (CFU-GM) progenitor cells (n = 30).1 Decision for marrow purging followed the general policy of individual centers: 94% of the patients receiving purged marrow were treated in four centers where marrow purging is institutional for autografting AML.

All teams reporting data for this study have performed ABMT after approval of their local ethical committee and/or in keeping with the laws and regulations of their country and always in conformance with the declaration of Helsinki.

Statistical methods. A series of pretransplant, peritransplant, or post-transplant variables were studied, including age, sex, FAB classification, nature and number of induction and consolidation courses given with a particular attention to high-dose cytosine arabinoside (Ara-C), pretransplant regimen, and marrow purging. Various intervals pretransplant were also studied as possibly reflecting a good prognosis (short interval from diagnosis to CR1) or possibly introducing a selection bias (long intervals from diagnosis to ABMT, CR to marrow collection, marrow collection to ABMT, and CR to ABMT).

Two studies were done to evaluate marrow purging, the first one comparing all patients receiving purged marrow to those receiving nonpurged marrow and the second considering separately patients receiving marrow purged with mafosfamide at a standard dose and patients whose marrows were treated with a dose of mafosfamide individually adjusted.

Leukemia-free survival (LFS) was defined as survival without evidence of leukemia. To evaluate the probability of relapse, patients dying either from direct toxicity of the procedure or from any other cause not related to leukemia were censored.

All analyses were done using BMDP statistical package.11 Differences between groups were studied using the χ² statistics for qualitative variables, Kaplan-Meier curves for LFS and probability of relapse were calculated using the product-limit method.12 Results are expressed in percentages ± standard error. Graphical presentation of curves was terminated when fewer than three patients remained at risk. The significance of differences between curves was estimated by means of the log-rank test (Mantel Cox) and the generalized Wilcoxon test (Breslow). Unless otherwise stated, results given for P values are those of the log rank tests.

Variables associated with relapse or LFS in univariate analyses with an arbitrarily selected P value less than .20 were entered into a multivariate analysis as variables of recognized interest. Multivariate analyses of prognostic factors were performed using the Cox proportional hazard regression model.13 Multivariate analyses were examined and adjusted for possible effects of delay between onset of remission and transplantation. Because this delay was heterogeneous and might have induced a selection bias, it was introduced both as a covariate in the regression model and as a stratification factor. Results on significance of prognostic factors were similar using the two methods. They were also similar whether the regression analysis was performed using a top-down or a bottom-up stepwise procedure.

All P values were two-tailed and, unless specified, were based on the results of multivariate analyses. Because comparisons of multiple factors were made, only P values ≤ .01 were considered significant; P values between .01 and .05 were considered to be of marginal significance and were presented only to show trends.

RESULTS

Overall results. For patients autografted in CR1, the overall LFS at 3 years was 39% ± 3%. The corresponding figures were 41% ± 4% in SR patients and 34% ± 9% in HR patients (P = .16). The actuarial probability of relapse at 3 years for the whole group was 55% ± 4%; the corresponding figures were 53% ± 4% in SR patients and 60% ± 9% in HR patients (P = .18). In the more homogeneous treated group of AML SR patients autografted in CR1 after TBI (n = 107), the LFS at 3 years was 45% ± 5%, and the probability of relapse was 47% ± 6% (Fig 1).

Factors associated with relapse. In the total population of patients autografted in CR1 (Table 2), five variables (FAB classification, presence of any poor risk factor, interval
from CR1 to ABMT, interval from CR1 to marrow collection and marrow purging) were associated with the probability of relapse in univariate analyses with \( P \) values < .20. The correlation between purge and relapse was stronger when considering three groups of patients (no purge versus purge with mafosfamide at standard dose versus purge with mafosfamide at levels individually adjusted; \( P = .007 \)), rather than two groups (no purge versus purge with mafosfamide at any dose; \( P = .05 \)).

In multivariate stratified analyses, all remained significant except the influence of risk factors. Within the FAB classification, results were worse in the M4 variety, with a probability of relapse of 65% ± 7% at 3 years versus 44% ± 13% in M3 (relative risk, 2.39; \( P = .001 \)). Long intervals from CR to ABMT were associated with lower probabilities of relapse: for intervals of 1 to 3 months, 4 to 6 months, 7 to 9 months, and above, they were 67%, 59%, 56%, and 35%, respectively, at 3 years (\( P = .005 \); Fig 2A). A similar relationship was observed for the interval from CR to marrow collection (\( P = .04 \)), which was included, however, in the interval from CR to ABMT. Marrow purging with mafosfamide at levels individually adjusted was significantly better than no purge (probability of relapse, 17% ± 7% versus 59% ± 4% at 3 years; relative risk, 0.23; \( P = .0002 \)). However, when marrow purging with all methods of in vitro treatment with mafosfamide (standard and adjusted doses) was compared with no purging, the difference that was significant in univariate analysis (relapses at 3 years; 40% ± 6% versus 59% ± 4%; \( P = .05 \)) was no longer significant in multivariate analyses. When the results of purging versus no purging were considered in relation to each CR to ABMT interval, purging appeared significantly more effective in shorter intervals (Fig 3A and B).

When considering the more homogeneous subgroup of patients with standard risk AML autografted after TBI as a unique pretransplant high dose regimen (Table 3), two variables were associated with \( P \) values < .20 in univariate analysis, and both remained significant in multivariate analyses; these were again the delay from CR1 to ABMT and marrow purging.

For the same intervals CR1 to ABMT, 1 to 3 months, 4 to 6 months, 7 to 9 months, and above 9 months, the relapse rates at 3 years were 64%, 47%, 50%, and 21%, respectively (\( P < .001 \); Fig 2C). In the group of patients receiving purged marrow (all doses combined), the relapse rates at 3 years were 21% ± 8% versus 55% ± 7% in the group receiving nonpurged marrow (relative risk, 0.34; \( P = .005 \)) (Fig 4A). When considering purging versus no purging for each interval from CR to ABMT, purging appeared to be significantly more effective in shorter intervals (Fig 3C and D) (\( P = .01 \)). Table 4 summarizes the 3-year relapse probabilities in the various populations studied according to whether marrow was or was not purged.

**Factors associated with LFS.** By univariate analyses, several variables were associated with \( P \) values < .20: five variables in patients CR1 (Table 2) and one in the group of patients CR1 SR autografted after TBI (marrow purging, \( P = .05 \); Table 3). In multivariate analyses, one variable appeared significant in CR1 (the FAB classification) and one in CR1 SR TBI (marrow purging).

Within the FAB classification, results in M4 were worse than in M3: at 3 years, the LFS for patients autografted in CR1 was 51% ± 10% for M3, while it was 30% ± 6% in M4 (\( P = .03 \)). As for the probability of relapse, the interval from CR to ABMT was correlated with LFS: longer intervals were associated with better LFS both in CR1 (\( P = .007 \)) and in CR1 SR TBI (\( P = .02 \)). In CR1, patients autografted more than 9 months post-CR had an LFS of 56% ± 10% at 4 years versus 40% ± 7%, 35% ± 5%, and 27% ± 8% in those transplanted 7 to 9 months, 4 to 7 months, and less than 3 months post-CR, respectively (Fig 2B). Similarly, in the group CR1 SR TBI, LFS for the same intervals were 60% ± 14%, 42% ± 12%, 38% ± 8%, and less than 33%, respectively (Fig 2D). Considering marrow purging, patients with AML CR1 SR TBI receiving marrow purged by mafosfamide (\( n = 30 \)) had a significantly better LFS than those receiving unpurged marrow (\( n = 77 \)) (LFS at 4 years, 63% ± 8% versus 34% ± 7%, \( P = .05 \)) (Fig 4B).

**Toxicity and causes of death.** A total of 163 complications were reported. Bacterial infection was the most frequent, occurring in 106 patients (40% of the 263 patients), followed by fungal (11.6%) and viral (10%) infections. Pneumonitis, veno-occlusive disease of the liver (VOD), and cardiac failure were reported in 2%, 2.6%, and 3% of the patients, respectively.

Considering the various pretransplant regimens, the overall incidence of complications was lower after FTBI than TBI (68.5% versus 76%; \( P < .0005 \)).

Patients receiving purified marrow had a slower recovery of
leukocytes (P < .001) and higher incidence of complications than those receiving unpurged marrow, globally (77% versus 55%, P < .001) and by subcategories (infections, 61% versus 32%, P < .0001; pneumonitis and liver VOD, 5.6% versus 1%, P < .05 for each). Of the 121 patients who died, 74 died as a direct consequence of leukemia, and 47 died of various combinations of causes not directly related to leukemia. In 21 cases, the toxicity of the pretransplant regimen was a major factor contributing to mortality.

Comparison of patients receiving purged and nonpurged marrow. The characteristics of all patients receiving purged and nonpurged marrow were studied. Despite the large number of centers involved, the induction and consolidation courses given in the pretransplant period were similar. For induction, all patients received 1 or 2 courses of a combination containing at least an anthracycline and cytosine arabinoside. The same drugs, 6 thioguanine, M Amsa and Vp 16, were used in various combinations for consolidation. We did not detect any difference between the two groups receiving purged and nonpurged marrow, either in the nature of drugs used or in the number of courses of induction and/or consolidation given (purge versus nonpurge number of courses of induction to reach CR: 1.74 ± 0.77 versus 1.73 ± 0.9; number of consolidation courses pre-ABMT: 1.96 ± 1.25 versus 2.18 ± 1.58; P = not significant). A total of 46 patients received intermediate or high dose Ara-C (≥ 4 g/m²) in the pretransplant period; 37 (80%) of them were autografted with nonpurged marrow. Of the 69 patients receiving purged marrow, 65 were treated in institutions where autografting with marrow purging was systematically applied to all patients, and, therefore, they were not selected. In one other institution, three patients of a total of six received purge marrow as part of a randomized protocol comparing purge with no purge. Finally, one patient receiving purged marrow was treated in a center reporting only one ABMT with no reported specific reason for purging. More patients with reported extramedullary localizations at time of initial diagnosis received purged marrow (44.1% versus 27.6% in the control group, P = .0007). The pretransplant intervals were similar in patients receiving purged and unpurged marrow: in the groups CR1 and CR1 SR TBI, 28% and 31.5%, respectively, of the patients transplanted within 6 months of achieving CR received purged marrow. Similarly, the figures were 22% and 21%, respectively, in those transplanted after 6 months (P = not significant).

Results of individual teams were analyzed separately and compared for possible center effects, with the hypothesis that centers performing purging might be more experienced and/or more adept at selecting or supporting patients, resulting, for instance, in better LFS for the patients receiving purged grafts, independent of the in vitro purging per se. We found no difference when comparing the bigger centers (more than 10 ABMTs reported for this analysis) to the nonpurge category. Small nonpurging centers (n = 22) contributed 37 ABMTs for this study (21% of the total population receiving nonpurged marrow); the LFS in these 37 patients did not differ significantly from LFS observed in the nonpurging bigger centers.

Characteristics of patients with SR AML autografted after TBI, including induction and consolidation with or
Probability of relapse

No purge
\( (n=48) \)

purge with Mafosfamide
\( (n=23) \)

Probability of relapse

No purge
\( (n=74) \)

purge with Mafosfamide
\( (n=21) \)

Probability of relapse

No purge
\( (n=27) \)

Fig 3. Cumulative probability of relapse after ABMT according to whether marrow was purged or not and according to whether the delay from remission to ABMT was less than 6 months or greater than 6 months. Patients with AML in CR1 (A and B), \( P = .002 \); patients with SR AML in CR1 autografted after TBI (C and D), \( P = .01 \).

Table 3. Variables Analyzed for Association With Probability of Relapse and LFS. Patients With SR AML in CR1 Autografted After TBI \( (n = 107) \)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Distribution* or Frequency</th>
<th>Association With Relapse†</th>
<th>LFS‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of transplant</td>
<td>1981-1986</td>
<td>.86</td>
<td>.95</td>
</tr>
<tr>
<td>Patient age</td>
<td>30 (2-51)</td>
<td>.64</td>
<td>.96</td>
</tr>
<tr>
<td>Male sex</td>
<td>44%</td>
<td>.84</td>
<td>.88</td>
</tr>
<tr>
<td>FAB classification</td>
<td>M1 to M5</td>
<td>.45</td>
<td>.34</td>
</tr>
<tr>
<td>Intervals (d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis to CR</td>
<td>55 (25-160)</td>
<td>.66</td>
<td>.35</td>
</tr>
<tr>
<td>CR to ABMT</td>
<td>140 (70-365)</td>
<td>.09</td>
<td>.29</td>
</tr>
<tr>
<td>Marrow purging with mafosfamide (all doses)</td>
<td>28.4%</td>
<td>.01</td>
<td>.05</td>
</tr>
<tr>
<td>Mafosfamide adjusted</td>
<td>21.1%</td>
<td>.026</td>
<td>.13</td>
</tr>
</tbody>
</table>

*Median and 5th to 95th percentiles.
†Significance levels from univariate analyses (Mantel Cox).

There was no indication of biased selection, other than a higher proportion of children in the group receiving purged marrow. We therefore studied separately four subgroups of patients in relation to age (children below 15 years of age, adults above 15, 30, and 45 years). Age was not a prognostic factor, either by univariate or by multivariate analysis when studying probability of relapse and LFS in both the CR1 and CR1 SR TBI groups.

In conclusion, we did not detect any selection bias that could explain differences in relapse rates and/or LFS between the two groups receiving purged and nonpurged marrow, which would be independent from the in vitro treatment of marrow per se. Indeed, the trend was in favor of higher risk patients receiving purged marrow and patients autografted with nonpurged marrow receiving more consolidation and being transplanted later.

DISCUSSION

The first attempts at ABMT in AML were done in end-stage disease. Despite a high rate of CR ranging from 55% to 90%, results were disappointing since all patients eventually relapsed and died. Since 1980, several teams reported on ABMT to consolidate patients with AML either in first or second CR, using different pretransplant regimens followed by reinfusion of purged or nonpurged marrow. Most of these reports were promising but concerned only small series of patients with a short follow-up, which prevented any interpretable analysis of the data.

The aim of the present study was to analyze the EBMT database on AML autografts and evaluate the possible impact of marrow purging. Several steps were taken to improve the quality of the data and to structure the analysis:

1. Before the study, all teams received a printout of their
MARROW PURGING IN AUTOGRAFTING FOR AML

4. It had been suggested that marrow purging might not bring any additional and/or detectable beneficial tumor cytoreduction in a situation where chemotherapy previously given to the patient would achieve a sufficient degree of so called “in vivo purge.” Therefore, we analyzed purging versus no purging, by intervals from CR to ABMT, postulating that the effect of purging might be more easily detectable, or alternatively, purging might be more effective, in patients transplanted earlier after fewer courses of consolidation chemotherapy following the induction of CR. This analysis produced some interesting results.

5. A careful comparison of the two populations, purge versus no purge, did not detect any selection bias. This study included an analysis of all chemotherapy induction and consolidation regimens given in the pretransplant period with a special attention to high dose Ara-C, a comparison of pretransplant intervals, and a search for a possible center effect.

This report is the first to show an effect of marrow purging with mafosfamide in AML. It also points out the influence of some other prognostic factors, such as the FAB classification, the nature of the pretransplant regimen, and the impact of the interval from CR to ABMT on relapse rate and LFS. In this study, marrow purging appeared to be beneficial. The efficacy of marrow purging was significant in the population of patients with AML CR1 SR autografted after TBI (probability of relapse at 3 years: 23% versus 55%, \( P = .005 \); LFS at 4 years: 63% versus 34%, \( P = .05 \)). Results of purging were particularly favorable in patients in this group autografted within 6 months of achieving CR (probability of relapse: 20% versus 61% at 3 years), while no improvement could be detected for a longer interval. Marrow purging also lowered the probability of relapse in the population of patients grafted in CR1 (all pretransplant regimens, SR and HR), but its benefit appeared only when considering apart the group of patients receiving marrow purged with doses of mafosfamide individually adjusted and essentially because of this group (probability of relapse in purge with doses adjusted, purge with standard doses, and no purge: 17%, 56%, and 59%, respectively; \( P = .0002 \) at 3 years). Marrow

Table 4. 3-Year Actuarial Probability of Relapse in Relation to Marrow Purging

<table>
<thead>
<tr>
<th>Population Studied</th>
<th>No Purge</th>
<th>Purge With Mafosfamide (constant + adjusted doses combined)</th>
<th>Purge (constant dose)</th>
<th>Purge (adjusted dose)</th>
<th>( P ) Univariate*</th>
<th>( P ) Multivariate†</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR1: no purge v purge</td>
<td>59 ± 4 (n = 194)</td>
<td>40 ± 6 (n = 69)</td>
<td>( 56 \pm 8 ) (n = 39)</td>
<td>( 17 \pm 7 ) (n = 30)</td>
<td>.007</td>
<td>.0002</td>
</tr>
<tr>
<td>CR1: no purge v purge constant v purge adjusted</td>
<td>59 ± 4 (n = 194)</td>
<td>65 ± 6 (n = 77)</td>
<td>23 ± 8 (n = 30)</td>
<td>( P ) Univariate*</td>
<td>( P ) Multivariate†</td>
<td></td>
</tr>
<tr>
<td>CR1 SR post-TBI</td>
<td>61 ± 7 (n = 50)</td>
<td>20 ± 9 (n = 23)</td>
<td>( P ) Univariate*</td>
<td>( P ) Multivariate†</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: NS, not significant.
*Mantel-Cox.
†Cox proportional hazard regression model.
Considered to be at higher risk. For instance, 44.1% of patients with reported extramedullary localizations at time of initial diagnosis had their marrow purged by mafosfamide, proportion of marrow purge in the groups of patients usually and unpurged marrow did not reveal any significant bias of selection; in fact, the trend was in favor of a higher CR2 than in CR1 (40.3% versus 26.6%; P = .0001). However, age did not appear as a significant prognostic factor in this study, and results in favor of marrow purging were still observed when studying separately children and adults. Therefore, it is quite unlikely that a lower relapse rate in patients receiving purged marrow reflects a selection bias.

The potential efficacy of mafosfamide to purge AML marrow is in agreement with several considerations. Cyclophosphamide (CY) derivatives are cytolytic to AML cells in numerous animal systems. In the Brown Norway myelocytic leukemia (BNML) rat model, which is very close to human AML, 4 hydroperoxycyclophosphamide (4HC) has been shown to purge tumor cells from normal marrow-tumor cell mixtures: animals given cell suspensions incubated with higher doses of 4HC survived lethal irradiation without the subsequent appearance of leukemia. Similar observations were later obtained with mafosfamide, a more stable CY derivative that generates 4HC in vitro. In addition, although CY is not a major agent in conventional induction regimens for human AML, it has remained the standard drug (combined with TBI) for conditioning patients before allogeneic transplantation. Therefore, despite the absence of a direct evaluation of tumor cells killing in each individual patient, it seems likely that marrow incubation with CY derivatives as performed by numerous teams of the EBMT at dosages that would correspond to nonachievable serum levels by in vivo infusion is, indeed, tumor cytoreductive.

Whereas marrow purging appeared beneficial on relapse rate and, to a lesser extent, on LFS, it induced a higher rate of complications, at least in part related to slower kinetics of recovery of hematopoiesis after ABMT have been already studied by numerous investigators, as well as within the EBMT.

It has been shown that kinetics are definitely slower in AML than in acute lymphocytic leukemia (ALL), and that further delays, especially in platelet recovery, are a possible consequence of purging with mafosfamide: in some patients, platelet support has been reported to be necessary for more than 1 year and even 18 months. Marrows collected in CR of AML have been shown to have low concentrations of megakaryocytic progenitors (CFU-Mega), and an intrinsic defect of the stem cell pool, which would not exist in ALL, has been postulated. Therefore, while marrow purging has...
reduced the probability of relapse, it also induces on the normal residual stem cell pool some toxicity of potential clinical consequence.

In our study, longer intervals from CR to ABMT were significantly associated with better LFS and lower relapse rates. The cut-off point was 9 months, with patients of the CR1 SR TBI group reaching an LFS at 3 years as high as 60% with a relapse rate of only 21%. This finding of a relationship between LFS and intervals pretransplant with a favorable impact of long intervals is not unexpected. Two explanations may be proposed. The first is a selection bias: patients transplanted late are more likely to be cured already by chemotherapy at the time when they are transplanted, and, therefore, the relapse rate is lower. Comparison of these patients with similar groups treated by conventional chemotherapy with LFS curves initiated only with those still in CR, 7 and 9 months post-induction, would be one way to test this hypothesis. For example, Juttner et al. reported, in a series of 59 patients with AML, an apparent LFS plateau of 23% if all patients are considered from initial diagnosis, increasing to 32% and 43% when only patients still in CR at 6 and 9 months, respectively, are evaluated. An alternate explanation is that patients transplanted late have received more courses of consolidation chemotherapy in the pretransplant period (data not shown). Whether these additional courses have had a direct impact by reducing the tumor load in the patient, or an indirect one by introducing a reduction in the contamination of the marrow collected (in vivo purging), or even both, cannot be distinguished. In both hypotheses, one would expect marrow purging to be less effective and/or more difficult to evaluate in patients transplanted late.

In conclusion, this study indicates that marrow purging with mafosfamide has an effective antileukemic property for ABMT in AML and in certain circumstances, such as CR1 or CR1 SR post-TBI. Its potential efficacy is more easily detectable when ABMT is done early after initiation of CR.

ACKNOWLEDGMENT

The authors are grateful to Patricia Palut for help in computer analysis and preparation of the manuscript.

REFERENCES


Autologous bone marrow transplantation for acute myelocytic leukemia in first remission: a European survey of the role of marrow purging

NC Gorin, P Aegerter, B Auvert, G Meloni, AH Goldstone, A Burnett, A Carella, M Korbling, P Herve and D Maraninchi