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AUTOLOGOUS STEM CELL TRANSPLANTATION IN ACUTE MYELOID LEUKEMIA

Factors Influencing Outcome. A 13 Year Single Institution Experience.

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SUMMARY

We report our results of autologous stem cell transplantation (SCT) in patients with AML during the last 13 years. Between August 1990 and December 2003, 42 patients with acute myeloid leukemia (AML) received an autologous SCT. Patients were classified as standard risk if first complete remission (CR) was induced after one or two chemotherapy regimens and the white blood cell count at presentation was below 50.000/mL (n=12), while patients requiring more than two induction regimens to attain first CR and with CR2 ou more advanced disease and/or had a higher white blood cell count at presentation were defined as high risk (n=30). Twenty one patients were transplanted in first CR. The median patient age was 24 years (range, 2 – 56 years), and the median time interval from diagnosis to autologous SCT was 9 months (range 3 – 87 months). The conditioning regimen for SCT consisted of busulfan (BU) 16 mg/kg and melfalan (MEL) 180 mg/m2 (BUMEL) in 17 (40%) patients and busulfan 16 mg/kg and VP-16 60 mg/kg (BUVP16) in 22 (52%) patients. Three patients received a different conditioning regimen with BCNU 300 mg/m2, VP16 2 g/m2 and melphalan 160 mg/m2 (BEM). Twenty five (60%) patients received bone marrow (BM), 11 (26%) patients received peripheral blood stem cells (PBSC) and 6 patients (14%) received BM plus PBSC. With a median follow-up of 7 years, the 13 year overall survival (OS) and disease-free survival (DFS) of all patients is 52% and 40%, respectively. In univariate analysis, males had a significantly superior DFS than females (55% *vs* 22%, p=0.003), and patients younger than 15 years of age had significantly superior OS and DFS than older patients (50% *vs* 35%, p=0.05; and 50% *vs* 28%, p=0.03, respectively). Patients with FAB M3 subtype also had a superior OS than the other FAB subtypes (100% *vs* 44%, p=0.05). There was a strong statistical correlation between risk group and survival. In fact, the patients with standard risk had a superior OS and DFS than those with high risk disease (67% *vs* 23%, p=0.0004; and 50% *vs* 27%, p=0.01, respectively). When patients with FAB M3 disease were excluded from the analysis, the group with standard risk continue to have a superior OS and DFS (67% *vs* 13%, p=0.008; and 50% *vs* 14%, p=0.02, respectively). We conclude that autologous SCT is an effective treatment in AML with the possibility of long survivorship, particularly in patients with standard risk disease.

Key words: Acute myeloid leukaemia, autologous stem cell transplantation

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R E S U M O

TRANSPLANTE AUTÓLOGO DE CÉLULAS ESTAMINAIS EM LEUCEMIA MIELÓIDE AGUDA.
Factores com Influência na Sobrevida. Experiência de 13 anos de uma Instituição.

Analisaram-se retrospectivamente os resultados do transplante autólogo com células progenitoras hematopoiéticas (TAPH) em doentes com leucemia mielóide aguda (LMA). Entre Agosto de 1990 e Dezembro de 2003, 42 doentes com LMA foram submetidos a TAPH. Os doentes foram classificados como tendo risco standard se a primeira remissão completa (RC) foi induzida com um ou dois ciclos de quimioterapia e apresentavam uma contagem de leucócitos inferior a 50.000/mL na altura do diagnóstico (n=12), enquanto que os doentes que necessitaram mais de dois regimes terapêuticos para obter primeira RC, em RC2 ou com doença mais avançada e/ou com uma contagem de leucócitos mais elevada foram classificados como tendo doença de alto risco (n=30). Vinte e um doentes foram transplantados em primeira RC. A mediana de idade dos doentes era de 24 anos (2 – 56 anos) e o intervalo de tempo mediano entre o diagnóstico e o transplante foi de nove meses (3 – 87 meses). O regime de condicionamento utilizado foi busulfan 16 mg/kg e melfalan 180 mg/m2 (BUMEL) em 17 (40%) dos doentes e busulfan 16 mg/kg e VP-16 60 mg/kg (BUVP16) em 22 (52%) dos doentes. Três doentes receberam um regime de condicionamento alternativo que consistiu em BCNU 300 mg/m2, VP-16 2 g/m2 e MEL 160 mg/m2 (BEM). Vinte e cinco (60%) dos doentes receberam medula óssea (MO), 11 (26%) doentes receberam células estaminais do sangue periférico (PBSC) e 6 (14%) doentes receberam MO e PBSC. Com um seguimento mediano de sete anos, a probabilidade de sobrevivência global (SG) e sobrevivência livre de doença (SLD) aos 13 anos foi de 52% e 40%, respectivamente. Na análise unifactorial, os doentes do sexo masculino tiveram uma SLD superior (55% *vs* 22%, p=0.003), e aqueles com menos de 15 anos de idade tiveram SG e SLD maior do que os doentes mais idosos (50% *vs* 35%, p=0.05; e 50% *vs* 28%, p=0.03, respectivamente). Os doentes com LMA-M3 da classificação FAB tiveram uma SG superior aos dos restantes subtipos (100% *vs* 44%, p=0.05). Verificou-se uma forte correlação estatística entre o grupo de risco e o padrão de sobrevivência. De facto, os doentes com risco standard tiveram SG e SLD superiores àqueles com doença de alto risco (67% *vs* 23%, p=0.0004; e 50% *vs* 27%, p=0.01, respectivamente). Quando se exluiu da análise os doentes com LMA-M3, o grupo de risco standard continuou a apresentar SG e SLD superiores em relação aos doentes de alto risco (67% *vs* 13%, p=0.008; e 50% *vs* 14%, p=0.02, respectivamente). Concluímos que o TAPH é um tratamento eficaz na LMA como a possibilidade de permitir sobrevida a longo prazo livre de doença, em particular nos doentes com risco standard.

Palavras Chave; Leucemia Mielóide Aguda, Transplantação Autóloga, Células Estaminais

INTRODUCTION

In the last two decades, the treatment of acute myeloid leukemia (AML) has evolved with the use of more aggressive therapeutic strategies[1,2]. Post-remission treatment remains a critical issue in this disease[3-5]. Although most institutions try to offer an allogeneic stem cell transplant (SCT) to patients with high-risk AML in first complete remission (CR), some patients do not have a suitable donor in the family or in the international registries. Therefore, autologous SCT after myeloablative chemoradiotherapy has also been widely used as consolidation treatment of patients with poor-prognosis AML[6-9].

Autologous SCT has several advantages and disadvantages in relation to allogeneic SCT. The prompt availability of the graft, the possibility of applying this procedure to older patients, the lower incidence of severe complications and the absence of graft-versus-host disease are positive factors. On the other hand, autologous SCT cannot be undertaken unless remission is achieved and the stem cells are cryopreserved, its success may be limited by the presence of malignant cells in the graft, there is no graft-versus-leukemia effect and the optimal timing and conditioning regimen remain controversial. Nevertheless, several studies have shown that autologous SCT com-

pares favourably with other post-remission strategies in patients with AML[6-8].

In this retrospective study, we report the results of patients with standard and high-risk AML who underwent autologous SCT in our institution over the last 13 years. We analyzed the effect of several important factors on overall survival (OS) and disease-free survival (DFS), including age, sex, white blood cell (WBC) count at diagnosis, French-American-British (FAB) classification subtype, disease state, risk group, stem cell source and conditioning regimen.

MATERIALS AND METHODS

Patients

Autologous SCT has been used in our institution as the consolidation treatment of all patients less than 60 years old with AML in first CR without inv 16, t (8;21) or t (15;17) cytogenetics and who lacked an adequately HLA-matched donor. All patients with more advanced disease (≥ second CR) and without an HLA-matched donor, regardless of their cytogenetic profile, were also submitted to an autologous SCT. In this analysis patients were classified as having standard risk if first CR was induced after one or two chemotherapy regimens and the white blood cell count at presentation was below 50.000/μL. Patients requiring more than two induction regimens to attain first CR (defined as primary induction failures), with more advanced disease and/or with a higher white blood cell count at presentation were defined as high risk. All patients with primary induction failure were eligible if they subsequently attained CR with a salvage induction regimen. Patients with a previous myelodysplasia diagnosed for more than 3 months and with secondary AML following chemotherapy given for another malignant disorder were excluded from this study.

Complete remission (CR) was defined by the presence of all the following characteristics: normal bone marrow (BM) morphology with less than 5% blasts, absence of circulating blasts, absence of extramedullary leukemic cell infiltration, a neutrophil count greater than 1.500/mL and a platelet count greater than 140.000/mL. Moreover, remissions were required to last for a minimum of 30 days before proceeding to stem cell harvest and subsequent transplant.

Between August 31, 1990 and December 31, 2003, 42 patients (23 males, 19 females) with AML received an autologous SCT. All patients gave written informed consent. The clinical characteristics of the patients are depicted in Tables 1 and 2. Their median age was 24 (2 – 56) years and more than half of the patients had FAB M2 or M4 subtypes (Table 1). Of the 42 patients, 10 were referred to us by other institutions and we do not have their WBC count at diagnosis. In the remaining 32 patients, the median WBC count at diagnosis was 17.000/μl. Nineteen of 32 patients had a WBC count higher than 15.000/μl and 6 patients had a WBC greater than 100.000/μl. Overall, only 18/42 (43%) patients had cytogenetic analysis at diagnosis. At the time of transplant, 21 of 42 patients (50%) were in first CR. The remaining 21 patients were transplanted in early first relapse (n=3), second CR (n=15), third CR (n=1) or more advanced stages of the disease (n=2) (Table 2). Because this study included a small number of patients and only 8/21 (38%) patients in first CR had cytogenetic analysis at the time of diagnosis, the impact of this factor could not be ascertained on survival. Of the 21 patients transplanted in first CR, 12 were classified as having standard risk and 9 as having high risk since they needed 3 or more chemotherapy regimens to attain first remission. Considering the whole group, 12/42 patients (29%) had standard risk and 30/42 patients (71%) had high risk disease.

Table 1 - Clinical characteristics of the patients

Characteristics	Value
Median age at transplant; Years (range)	24 (2 – 56)
Sex; Male / Female	23 / 19
FAB classification	
M0	2
M1	3
M2	16
M3	6
M4	10
M5	3
M6	1
M7	1
Median WBC count at diagnosis, x 10^9/L (range)	17 (0.6 – 144.4)*

* in 32/42 patients

Table 2 - Clinical characteristics of the patients

Characteristics	Value
Median interval diagnosis to SCT; Months (Range)	9 (3 – 87)
Disease state of AML at SCT	
First CR	21*
Second CR	15
Third CR	1
≥ 4th CR	2
First relapse	3

9/21 patients in first CR were classified as having primary induction failure

The median time from diagnosis to SCT of the whole group was 9 months and 22 patients (52%) received the autologous SCT within 3 months of achieving CR. The 21 patients in first CR were transplanted a median of 3 months after the documentation of remission.

Conditioning Regimen, Growth Factors and Hepatic Veno-Occlusive Disease Prophylaxis

The patients were treated consecutively with two dif-

ferent protocols. The first 17 patients received busulfan (Bu) 1 mg/kg PO every 6 hours for 4 days (total dose 16 mg/kg) and melfalan (Mel) 90 mg/m2 IV for 2 days (total dose 180 mg/m2), on days –3 and -2 (BUMEL). After November 1996, 22 patients were treated with Bu (total dose 16 mg/kg, as above) on days –7 through –4 followed by intravenous infusion over 12 hours of VP-16 60 mg/kg on day -3 (BUVP16). In 3 patients, the protocol regimen was not deemed appropriate due to expected inefficacy or toxicity and they received BCNU 300 mg/m2 IV on day –7 followed by intravenous infusion over 12 hours of VP16 2 g/m2 IV on day -6 and MEL 80 mg/m2 IV for 2 days (total dose 180 mg/m2) on days –4 and -3 (BEM).

Regarding the administration of G-CSF post-transplant to hasten engraftment, 3/18 (17%) patients in the BUMEL arm, all 21 (100%) patients in the BUVP16 arm and all 3 (100%) patients in the BEM arm received G-CSF 10 mg/kg/day from day +1 until documentation of a granulocyte count greater than 1.000/mL for three consecutive days.

As prophylaxis of hepatic veno-oclusive disease (VOD), all patients conditioned with BUMEL received pentoxifiline 500 mg/d by continuous infusion and the patients treated with BEM and BUVP16 received prostaglandin E1 0.5 mg/d by continuous infusion from day – 7 until day + 21.

Source of graft

Transplantation of bone marrow (BM) progenitor cells was performed in 25 patients whereas in 11 patients peripheral blood stem cells (PBSC) were used. The remaining 6 patients underwent transplantation with a combination of BM and PBSC due to a low CD34+ cell count obtained in the apheresis. All 18 patients that were conditioned with BUMEL received BM whereas for the patients conditioned with BUVP16, 11 received PBSC, 6 received BM and 4 received BM plus PBSC. The remaining three patients conditioned with BEM received PBSC (n=2) and BM plus PBSC (n=1).

Infection Prophylaxis

All patients were isolated in high-efficiency particulate air-filtered positive-pressure air-flow rooms during the period of pancytopenia associated with the conditioning regimen and after autologous SCT. Prophylactic oral antibiotics against gram-negative bacteria and fluconazol 400 mg/day were started on day –4 and continued until ANC 500/ml. Oral acyclovir 800 mg bid was started on day –5 and continued until 3 months after transplantation. Pneumocystis carinii prophylaxis was maintained with oral trimethoprim-sulfamethoxazole 960 mg twice daily three days per week until 12 months after transplantation

Statistical analysis

Data was analyzed as of December 31, 2004. All patient details were routinely introduced and analyzed with the StemSoft software database (Stem Cell Technologies Inc, Vancouver, BC, Canada). Primary end points were treatment--related mortality (TRM), relapse, DFS and OS. TRM was defined as death during a continuous CR or death in the first 100 days after transplantation. Relapse was defined as persistent or recurrent disease. DFS was defined as survival without evidence of disease. For analysis of DFS, relapses or deaths from any cause were considered as events. For analysis of OS, events were deaths from any cause. Patients were censored at the time of last follow-up. Survival curves were plotted following the Kaplan-Meier method[10] and differences between the curves were analyzed with the log-rank test[11]. The following parameters were analyzed for their impact on the outcome: sex, age, initial white blood cell (WBC) count, FAB classification (M3 versus other FAB subtypes), number of courses needed for CR achievement (1 versus 2 or more), number of consolidation courses, graft source, disease stage at the time of transplantation and type of conditioning regimen. We tested the proportional hazards assumption for each factor in the Cox model using time-dependent covariates.

RESULTS

Engraftment

Overall, 37 of 42 patients (88%) achieved a sustained granulocyte count greater than 500/μL and 1.000/μL a median of 15 (9 - 54) and 17 (9 - 55) days after transplantation, respectively. In 33 of 42 (78%) patients, the median time to a self-sustained platelet count higher than 20 and 50 x 10^9/L was 38 (12 – 109) and 60 (15 – 200) days, respectively. The patients not included in these results died before achieving the mentioned neutrophil and platelet counts.

The time to engraftment depended on the source of stem cells and it was faster in recipients of PBSC. The patients transplanted with BM, PBSC and the combination of BM plus PBSC attained a neutrophil count greater than 500/μL a median of 33, 13 and 15 days post-transplant, respectively. Similarly, the same subgroups of patients achieved a platelet count greater than 20 x 10^9/L a median of 41, 31 and 33 days after the stem cell infusion, respectively.

Transplant-related mortality

Overall, 6 of 42 (14%) patients died with transplant-

-related causes; 1 (2%) patient was in CR1 and 5 (11%) patients had more advanced disease. Two patients in the BUMEL arm died within 100 days of transplant: 1 with cardiac toxicity at day + 13 and 1 with hepatic VOD at day +22. Of the patients treated with BUVP16, 4 died early post-transplant: 1 with severe sepsis at day + 10, 1 with hepatic VOD at day + 31, 1 with relapse at day +32 and 1 patient with organ failure at day +34.

Relapse and causes of death

The 12-year probability of relapse was 48% ± 8 for the entire group of patients (data not shown). Leukemia progression was the direct cause of death in 13/42 (31%) patients. Table 3 lists the cause of death in all patients.

Table 3 - Causes of death

Causes of Death	Nº patients (% of total)
Disease progression	13 (31%)
Hepatic Veno Occlusive Disease	2 (4%)
Interstitial pneumonia	2 (4%)
Infectious complications	2 (4%)
Organ failure	2 (4%)
Hemorrhage	1(2%)
Cardiac toxicity	1 (2%)

Overall survival and disease free survival

Table 4 lists the probabilities of OS and DFS in all the patients not adjusted for differences in factors that influence transplantation outcome. In univariate analysis, WBC count at diagnosis, source of graft and conditioning regimen did not have any impact on the probability of DFS or OS. Four factors emerged as statistically significant for survival in univariate analysis: age, sex, FAB subtype and disease risk group (Table 4).

With a median follow-up of 7 years, the 13-year Kaplan-Meier estimate of OS and DFS after SCT for the whole group of patients was 52% and 40%, respectively (Figure 1A and B).

Patients younger than 15 years of age had a significantly better OS (50% *vs*. 35%, p=0.05) and DSF (50% *vs*. 28%, p=0.03) than older patients. Males also had a significantly superior DFS than females (55% *vs*. 22%, p=0.003). All 6 patients with M3 subtype were submitted to transplant in second CR and 5/6 remain in continuous complete molecular remission after the autologous SCT. One patient relapsed and is currently 5 years after a related haplotype-disparate SCT, also in continuous molecular remission. The patients with FAB M3 disease had a significantly better OS than other FAB subtypes of AML (100% *vs*. 44%, p=0.05).

Table 4 - Univariate analysis of variables influencing DFS and OS

	Number Patients	OS (%)	DFS (%)
Median age at diagnosis			
< 15 Years	8	50 ± 20	50 ± 20
≥ 15 Years	34	35 ± 9	28 ± 10
P		0.05	0.03
Sex			
Male	23	58 ± 10	55 ± 11
Female	19	45 ± 13	22 ± 9
P		0.20	0.003
Median WBC count at diagnosis			
< 15 x 10^9/L	13	46 ± 15	31 ± 13
≥ 15 x 10^9/L	19	43 ± 13	42 ± 14
missing data	10		
P		0.91	0.24
FAB classification			
M3	6	100%	83 ± 15
Others	36	44 ± 9	34 ± 8
P		0.05	0.10
Disease status at SCT			
Standard Risk	12	67 ± 14	50 ± 18
High Risk	30	23 ± 9	27 ± 9
P		0.0004	0.01
Disease status at SCT (no M3)			
Standard Risk	12	67 ± 14	50 ± 18
High Risk	24	13± 7	14 ± 7
P		0.008	0.02
Source of stem cell			
BM	25	46 ± 11	41 ± 11
PBSC	11	63 ± 17	44 ± 15
BM + PBSC	6	67 ± 19	33 ± 25
P		0.82	0.66
Conditioning regimen			
BUMEL	18	36 ± 12	28 ± 10
BEM	3	67 ± 27	67 ± 27
BUVP16	21	65 ± 11	46 ± 12
P		0.46	0.09

There was a strong impact of the disease risk group on the probability of OS and DFS (Table 4). As depicted in Fig 2A and B, patients with standard risk had a significantly superior OS and DFS than those with high risk disease (OS - 67% *vs*. 23%, p=0.0004; DFS - 50% *vs*. 27%, p=0.01). Since all the patients with FAB M3 subtype were transplanted in second CR, they were classified in the high risk group. When these 6 patients were excluded from the analysis, the differences in OS and DFS according to risk group were also statistically significant (OS - 67% *vs*. 13%, p=0.008; DFS - 50% *vs*. 14%, p=0.02) (Fig 3A and B).

We also observed a trend for a better DFS in patients treated with the BUVP16 regimen in comparison with those

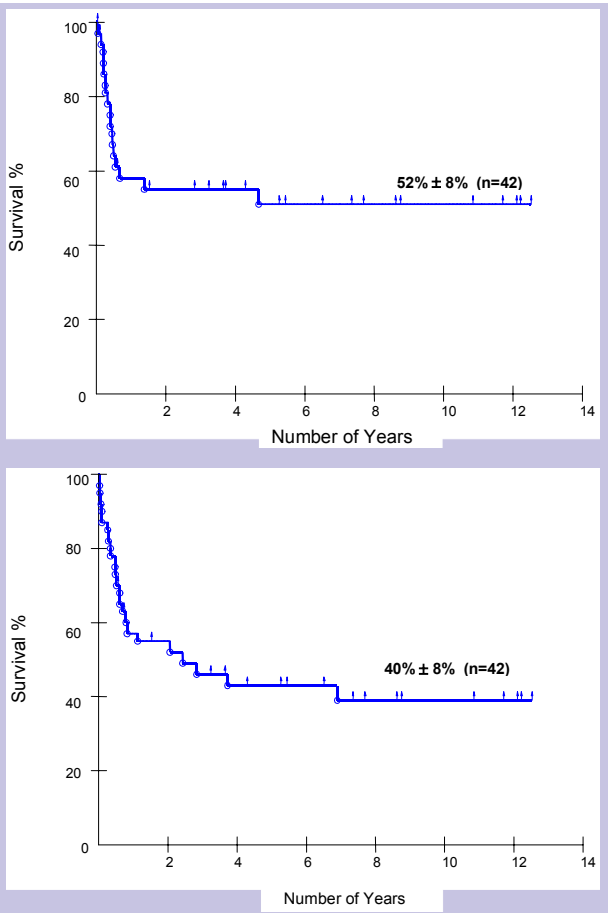

Fig. 1 - Kaplan-Meier estimates of OS (Fig 1A) and DFS (Fig 1B) at 13-years in all patients

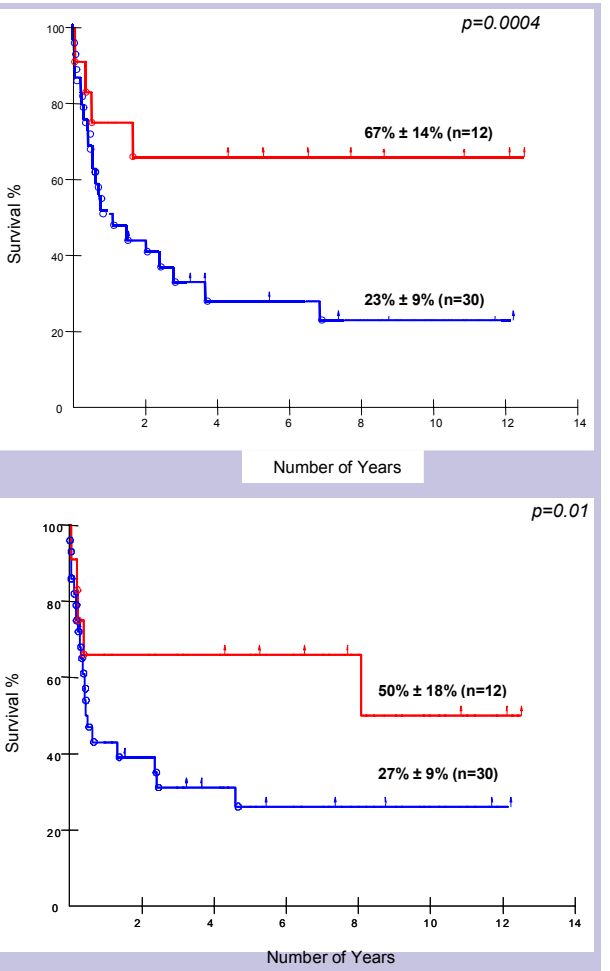

Fig. 2 - Kaplan-Meier estimates of OS (Fig 2A) and DFS (Fig 2B) at 13-years according to risk group at SCT in all patients

conditioned with BUMEL (46% *vs*. 28%, p=0.09) (Figure 4B). The subgroup of 13 patients with the FAB M4 and M5 variants showed a trend for a more favourable effect of BUVP16 on the probability of OS and DFS (data not shown).

All the patients transplanted with PBSC also received growth factors after transplantation. Despite the faster engraftment of neutrophils and the decrease in the number of days of intravenous antibiotics and of hospital stay, we did not find any influence in OS or DFS in relation to patients transplanted with BM and without growth factors post-transplant (data not shown).

DISCUSSION

Intensive combination chemotherapy as primary treatment of acute leukemia leads to a complete remission in the majority of the patients. However, despite subsequent treatments intended to maintain such remission, most patients relapse within 2 to 3 years of initial presentation[12]. In the last two decades, autologous SCT has been used to consolidate a substantial number of patients with poor prognosis AML who do not have an adequately HLA--compatible related or unrelated donor[13-15].

Our retrospective study analyzed the role of autologous SCT in patients with AML, mostly with poor--prognostic features. Although this study has a small number of patients, it shows long-term results with 7 years of median follow-up. Therefore, patients not relapsing at this late timing post-transplant have a high likelihood of being cured.

Overall, the results obtained in patients with standard risk are quite encouraging and clearly superior to the results achieved with chemotherapy alone post-remission in ours and other institutions.[1,3,4] However, the results in patients with high risk disease, excluding those with FAB M3 AML, were dismal and not superior to published results of chemotherapy alone after attaining CR. [4,13] Therefore, patients with poor prognosis AML lacking an adequately HLA-matched donor should probably be offered an allogeneic SCT from an alternative unrelated donor or

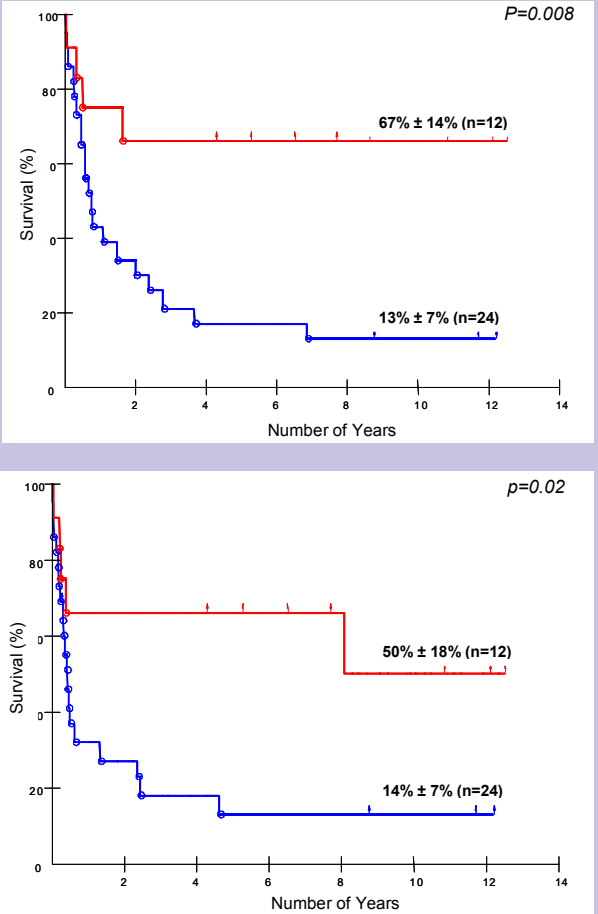

Fig. 3 - Kaplan-Meier estimates of OS (Fig 3A) and DFS (Fig 3B) at 13-years according to risk group at SCT in the 36 patients without FAB M3 AML

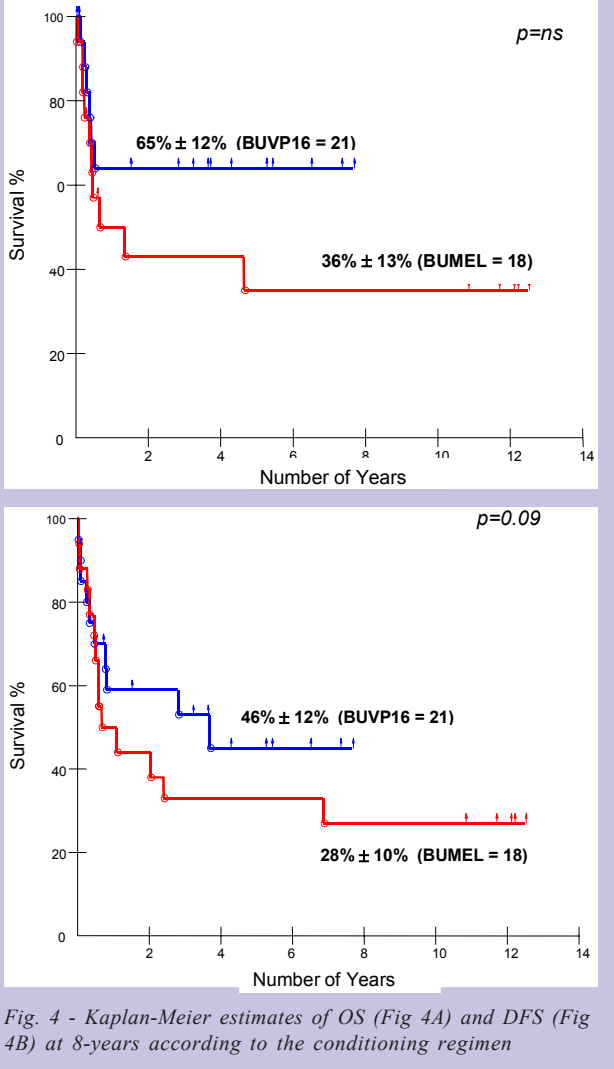

Fig. 4 - Kaplan-Meier estimates of OS (Fig 4A) and DFS (Fig 4B) at 8-years according to the conditioning regimen

from a haplotype-mismatched related donor.

The TRM observed in our group was 14%, which is higher than one would expect in a series of relatively young patients submitted to autologous SCT. However, considering that 50% of the patients were not in first CR at the time of transplant, the TRM observed is acceptable and comparable to other series[16]. All our patients received prophylaxis for hepatic VOD and, in fact, only 2 patients died with this complication.

One of major biases of retrospective studies of patients who undergo transplantation is the time-censoring effect, that is, patients who are transplanted late after the achievement of CR and that may be at low risk for relapse.[9,17-19]. In our study group, more than half of patients were autografted within 3 months from CR, and only 3 patients were transplanted more than 7 months from CR, which avoided the risk of including "cured" patients.

Since our study extends over 13 years, some of our protocols changed according to the international tendencies. This is the reason why there is some heterogeneity regarding the source of stem cells and the use of G-CSF post-transplant. Initially, the shift towards the increasing use of PBSC grafts in autologous SCT for acute leukaemia was also associated with the hope that the relapse rate would be smaller. However, this expectation has not been substantiated[20-22]. In our series, although the recipients of PBSC and of G-CSF post-transplant had fewer days of fever, of intravenous antibiotics and of hospitalization days, we did not observe any impact in their survival or relapse patterns.

We did not find a different survival pattern dependent on the initial leukocyte count. Since we do not have the WBC count at presentation of 10 patients, as they were referred to our institution more than a decade ago and this data is currently unavailable, it is unclear whether the inclusion of these data would change the results of this particular item. Similarly, we were not able

to evaluate the effect of poor-risk cytogenetics at presentation in the probability of survival, since a significant number of patients were not evaluated at the time of diagnosis.

The few patients treated with less than 15 years of age had a superior OS and DFS than older patients. However, there were not more young patients in the good risk group than in the high risk group. Similarly, we do not have an explanation for the higher survival of males in relation to females, since the distribution according to sex was even between the two risk groups. Likewise, there were not more males or young patients with FAB M3 or standard risk disease that could account for these statistical significant differences. Therefore, we hypothesize that other factors which we were not able to evaluate at the time of diagnosis, namely the cytogenetic profile and the white blood cell count, may have accounted for these differences.

The 6 patients with acute promyelocytic leukemia had the lowest probability for relapse and the best chance for DFS after autologous SCT, even though all of them were in second CR at time of transplant. We felt that it was adequate to include these patients in the current analysis since all of them were considered to be high-risk patients due to advanced disease. In fact, these results in acute promyelocytic leukaemia are not unusual and the same phenomena have been observed by other investigators[23, 24].

The number of consolidations pre-transplant performed before the transplant in patients in first CR did not had any influence on DFS. Therefore, based on our results, one course of consolidation in AML is sufficient if the patient is going to be submitted to an autologous SCT.

Although the BUVP16 regimen appeared to have been superior to the BUMEL regimen, it did not attain statistical significance. While more patients in the BUMEL arm than in the BUVP16 arm were transplanted in first CR (68% *VS* 33%, respectively), all patients with M3 AML were transplanted after conditioning with BUVP16. Therefore, it is difficult to establish a superiority of the latter regimen. It is known that the combination of BU and VP16 has excellent antileukemic activity and exhibits a synergistic cytocidal effect on HL-60 cell in vitro[25].

In summary, despite the lack of a graft-versus-leukemia effect, autologous SCT is a recognized therapeutic option for AML patients without donor. Our data are consistent with others reports showing the ability of autologous SCT to generate long-term DFS in patients with AML, particularly in those with standard risk disease [26,27].

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