AUTOLOGOUS TRANSPLANTATION OF GRANULOCYTE COLONY-STIMULATING FACTOR-PRIMED BONE MARROW IS EFFECTIVE TO SUPPORT MYELOABLATIVE CHEMOTHERAPY IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES AND POOR PERIPHERAL BLOOD STEM CELL MOBILIZATION.


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ABSTRACT

We assessed the hematopoietic recovery and transplant-related mortality (TRM) of patients who had failed peripheral blood stem cell mobilization and subsequently received high-dose chemotherapy supported by G-CSF-primed bone marrow (BM). Eighty-six heavily pretreated consecutive patients with acute leukemia (=21), refractory/relapsed non-Hodgkin’s lymphoma (=41) and Hodgkin’s disease (=17), and multiple myeloma (=7) were studied. Seventy-eight patients showed insufficient mobilization of CD34+ cells (<10 cells/µL) whereas 8 patients collected < 1x10^6 CD34+ cells/Kg. BM was primed in vivo for 3 days with 15-16 µg/Kg of subcutaneous G-CSF. Median numbers of nucleated cells, CFU-C and CD34+ cells/Kg harvested were 3.5x10^8, 3.72x10^4 and 0.82x10^6, respectively. Following myeloablative chemotherapy, median times to achieve a granulocyte count >0.5x10^9/L and an unsupported platelet count >20 and 50x10^9/L were 13 (range; 8-24), 15 (12-75) and 22 (12-180) days for lymphoma/myeloma patients and 23 (13-53), 52 (40-120) and 90 (46-207) days for leukemia patients. Median times to hospital discharge after transplant were 17 (12-40) and 27 (14-39) days for lymphoma/myeloma and acute leukemia patients, respectively. TRM was 4.6% whereas 15 patients died of disease. G-CSF-primed BM induces effective multilineage hematopoietic recovery after high-dose chemotherapy and can be safely used in patients with poor stem cell mobilization.
INTRODUCTION

Transplantation of autologous mobilized peripheral blood stem cells (PBSC) has largely replaced conventional, unprimed, bone marrow (BM) transplantation due to a faster hematopoietic reconstitution, earlier hospital discharge and saving of financial resources (1, 2). Prospective studies have also demonstrated accelerated engraftment when PBSC are transplanted in allogeneic recipients (3-5). Administration of granulocyte colony-stimulating factor (G-CSF), alone or in combination with cytotoxic drugs, is widely considered the most effective treatment to increase the number of circulating CD34+ stem cells. However, despite the superiority of mobilized blood, PBSC transplantation has some limitations. In particular, there is a general consensus that the number of CD34+ cells infused correlates with the rate of hematopoietic reconstitution (1). Therefore, below the minimum threshold level of 1x10^6 CD34+ cells/Kg reinvested, the risk of delayed hematopoietic recovery and increased transplant-related mortality (TRM) is high (6). Conversely, patients receiving at least 2x10^6 CD34+ cells/Kg show a rapid granulocyte recovery and patients infused with 5x10^6 CD34+ cells/Kg or more have multilineage fast engraftment (7). Thus, the number of CD34+ cells collected and transplanted is crucial to ensure a safe procedure.

Moreover, 10-30% of patients do not mobilize sufficient PBSC to proceed to transplant depending on the amount of previous chemoradiotherapy and the interval between chemotherapy and mobilization, marrow fibrosis or marrow involvement by the disease, addition of hematopoietic cytokines, and the number of pre-mobilization circulating progenitor cells (8-13). However, not all reasons for poor mobilization are known, since some heavily pretreated patients or patients with marrow metastases or fibrosis mobilize well whereas some normal donors mobilize poorly (14). Patients with absent or poor PBSC mobilization undergoing high dose therapy supported by BM cells do show delayed hematopoietic recovery and increased procedure-related morbidity and mortality (6). Thus, there are major concerns on the safety of autologous transplant in such patients. Recently, several reports (15-23), including randomized studies (15, 16), have shown that transplantation of G-CSF-primed BM induces a comparable engraftment to that of PBSC in both
autologous and allogeneic settings. Moreover, allogeneic recipients experienced reduced severity of acute graft-versus-host disease (GVHD) and less chronic GVHD (16). Based on these findings, we conducted a multicenter prospective study to assess the hematopoietic recovery and TRM of patients with hematological malignancies who had previously failed PBSC mobilization and received high-dose chemotherapy supported by G-CSF-primed BM. Patients were defined as poor mobilizers if the peak value of CD34+ cells during mobilization was lower than 10 cells/µL or in case stem cell collection <1x10^6 CD34+ cells /Kg (6). The minimum threshold of circulating CD34+ cells was chosen upon our own and others (24) experience indicating the minimum peak number of CD34+ cells predictive of a successful collection (i.e. ≥ 2x10^6 CD34+ cells/Kg body weight) as 10 cells/µL. In patients with less than that value is unlikely the collection of the target CD34+ cell dose with few aphereses (25). Poor mobilizers were studied because the lack of autologous stem cells poses important questions for the clinical management of patients for whom autologous transplantation has proven to be clinically beneficial. Our results, indicate that activated BM induces effective multilineage hematopoietic recovery and low TRM after high dose chemotherapy and can be safely used in patients submitted to autologous transplant programs.
PATIENTS AND METHODS

Patients

Eighty-six heavily pretreated consecutive patients undergoing autologous G-CSF-primed BM transplantation between February 1995 and December 2002 were studied in three transplant centers: Bologna (=40), Udine (=33) and Reggio Emilia (=13). The patient diagnoses, sex, median age, median number of lines of prior chemotherapy, the percentage who received prior radiotherapy and disease status at transplant are listed in Table 1. Patients were enrolled in the study if they were eligible for autologous stem cell transplantation according to our institutional guidelines and PBSC were not available (see below). Exclusion criteria, were: contraindication to BM harvest by general anesthesia, major organ dysfunction, myelosuppressive chemotherapy within 4 weeks of BM harvest, administration of any hematopoietic cytokine within 2 weeks before BM collection and pelvic radiation before stem cell collection. Patients with a positive test for human immunodeficiency virus (HIV) or any form of active hepatitis were also excluded. Notably, no exclusion criteria were set on the basis of the CD34+ stem cell content of BM harvest. All individuals gave written informed consent and the protocol was approved by the Hospital ethical committees.

Mobilization regimens

Sixty-six patients (lymphoma/myeloma = 63; acute leukemia =3) attempted PBSC mobilization by administration of 7.5 µg/Kg body weight twice a day of G-CSF (filgrastim, Granulokine, Roche, Milan or Neupogen, Dompè-Biotec, Milan, Italy) for 5-6 days whereas 20 patients (acute leukemia =18; lymphoma/myeloma =2) received priming chemotherapy followed by daily injection of 5 µg/Kg of G-CSF (filgrastim, Roche/Dompè). Patients with lymphoproliferative disorders were treated with cyclophosphamide 7 g/m² while acute myeloblastic leukemia (AML) patients were mobilized during the second consolidation course which generally included fludarabine, mitoxantrone and cytarabine (FLAN). Study patients were defined as poor mobilizers (=78) if the
peak value of circulating CD34⁺ cells was below 10 cells/µL. Eight patients showed a peak value of CD34⁺ cells slightly greater than 10 cells/µL; however the minimum CD34⁺ cell dose of 1x10⁶/Kg was not reached with 2 or 3 aphereses and the clinical investigator thought it would be unlikely to reach that cell dose with few additional collections (Table 1). Regardless of the mobilization strategy, PBSC collection was attempted after a minimum of 4 weeks from the last chemotherapy cycle (median 48 days; range 35-56).

**BM priming, collection and cell processing**

BM priming was performed with G-CSF (filgrastim, Roche/Dompè Biotec) at the dose of 7.5-8 µg/Kg twice a day for 3 days. BM cells were harvested on day +4 using standard procedures (15-20 mL of BM/Kg body weight) and frozen in 10% dimethyl sulfoxide using controlled-rate liquid nitrogen freezing (26). The minimum number of BM cells required to proceed to autotransplant was 1x10⁸ nucleated cells/Kg actual patient body weight. All patients submitted to BM harvest did achieve this threshold. At the time of reinfusion, BM cells were rapidly thawed at 37°C at bedside and reinfused via a central line (26).

**Progenitor cell assays**

Total nucleated cells, day 14 colony forming-unit cell (CFU-C) and CD34⁺ cells were assayed on BM collections as previously reported (26-28). In brief, CFU-C were scored by plating in duplicate 1x10⁵ light density cells in a total volume of 1mL of Iscove’s modified Dulbecco’s medium (Gibco, Grand Island, NY, USA) added with 20% fetal calf serum (Stem Cell Corp., Vancouver, Canada), and 1.1% (final concentration) methylcellulose. Colony-stimulating activity was provided by 10% (v/v) of a selected lot of phytohemagglutinin-lymphocyte-conditioned medium. Colonies were counted after 14 days of incubation at 37°C in a humidified 5% CO₂ atmosphere. CD34⁺ cell count was determined by flow cytometry (26, 27). BM cells were incubated at 4°C for 30 minutes with the anti-CD34 phycoerythrin-conjugated monoclonal antibody HPCA2 or an irrelevant isotype.
matched control antibody (Becton Dickinson, Milan Italy). Immunofluorescence analysis was performed using a FACScan equipment (Becton Dickinson). A minimum of 10,000 events were collected in list mode on FACScan software.

Conditioning regimens, supportive care and clinical monitoring

Four different disease-specific preparative regimens were used in this study. Carmustine, cytarabine, etoposide and cyclophosphamide (BAVC) (26) were administered to non-Hodgkin’s lymphoma patients (NHL). Hodgkin’s disease (HD) patients received myeloablative therapy that included carmustine, cytarabine, etoposide and melphalan (BEAM) (26). Acute leukemia and multiple myeloma (MM) patients were prepared with busulphan and cyclophosphamide (29, 30) and high dose melphalan (28), respectively. After completion of the conditioning regimen, patients were reinfused with autologous cryopreserved marrow cells (day 0).

All lymphoma/myeloma patients received 5µg/Kg/day of G-CSF starting day +6 post autograft. G-CSF was also used at 5µg/Kg/day in 18/21 acute leukemia patients upon clinical indication. Uniform supportive care measures were used for all patients on the study. Patients were nursed in single or double rooms in reverse isolation and received antimicrobial prophylaxis that consisted of oral nystatin and ciprofloxacin. Packed red blood cells and platelet transfusions were administered to maintain a hemoglobin level greater than 8 g/dL and a platelet count greater than 10x10^9/L. Patients were treated with broad-spectrum antibiotics when fever developed and the absolute neutrophil count (ANC) was less than 0.5x10^9/L. Amphotericin B (1mg/Kg/day) was added if patients had persistent fever after 4-7 days of intravenous antimicrobial therapy.

Patients underwent daily assessment of symptoms and physical examination during hospitalization and weekly after discharge. As previously reported, laboratoty studies were obtained before transplant, daily while in the hospital and weekly after discharge.
Hematopoietic recovery and clinical end points

The primary end point of the study was time to hematopoietic reconstitution, which was defined as the number of days to achieve an absolute neutrophil count (ANC) greater than 0.5x10^9/L (first of 3 consecutive days) and an unsupported platelet count greater than 20 and 50x10^9/L. Secondary end points were incidence of documented infections, use of intravenous antibiotics, days to hospital discharge after transplant and TRM. Assessment of tumor response to autologous transplant was generally performed 30 days after reinfusion and was planned every 2 to 4 months thereafter.

Statistical analysis

The results are presented as median values and ranges where applicable. The probabilities of neutrophil and platelet recovery and overall survival of the different series of patients were compared by means of the Kaplan and Meier method. Differences with p values less than 0.05 were considered statistically significant. The association between the number of CD34^+ cells infused and the time to hematopoietic recovery was assessed by the Pearson correlation test.
RESULTS

Study Patients
Between February 1995 and December 2002, 86 heavily pretreated consecutive patients were enrolled in this study. All together, patients for whom PBSC were not available represented 12.5% of all individuals submitted to PBSC mobilization in the three participating Institutions upon the study period. In particular, mobilization failure, according our stringent criteria, was observed in 58/573 (10.1%) lymphoma, 7/80 (7.3%) multiple myeloma and 21/35 (60%) acute leukemia patients.

Table 1 reports patient demographics and some of the most important clinical parameters widely considered to affect BM function such as diagnosis (i.e. acute leukemia vs lymphomas and MM), burden of previous chemotherapy and radiotherapy.

Sixty-six patients (lymphoma/myeloma = 63; acute leukemia =3) had failed PBSC mobilization with high dose G-CSF alone whereas 20 patients (acute leukemia =18; lymphoma/myeloma =2) received priming chemotherapy followed by G-CSF. Seventy-eight patients were defined as poor/non mobilizers because the peak value of circulating CD34+ cells was < 10 cells/µL. Eight additional patients did not collect the minimum CD34+ cell dose of 1x10⁶/Kg (Table 1).

BM harvest
Stem cell collection was performed after a minimum of 4 weeks from PBSC mobilization failure (median, 43 days; range, 32-95). G-CSF treatment was well tolerated and no patient required the reduction or suspension of the cytokine administration. Table 2 shows the number of nucleated cells, CFU-C and CD34+ cells collected after 3 days of priming of G-CSF and those recovered and reinfused after cryopreservation. No differences were noted between lymphoma/myeloma patients and leukemia patients as for nucleated cells and CFU-C collected. Conversely, lymphoma/myeloma patients showed a trend toward a higher number of CD34+ cells in BM grafts (p =0.07) (data not...
shown). Of note, the median number of CD34+ cells reinfused was 0.70 x 10^6/Kg with one patient receiving as little as 0.12 x 10^6 CD34+/Kg.

Because G-CSF is a hematopoietic cytokine which has been shown to induce proliferation of tumor cells, especially myeloid leukemic cells, the effect of G-CSF on BM tumor cell contamination were also evaluated. Six out of 7 myeloma patients had a plasma cell infiltration lower than 30% before BM harvest which was not modified by the cytokine treatment whereas no lymphoma patients showed BM infiltration at the time of stem cell collection (data not shown). Three leukemic patients had both molecular and cytogenetic markers at diagnosis which could be traced: inv(16), t (8;21) in acute myeloblastic leukemia (AML) patients and bcr-abl rearrangement in one case of Ph+ acute lymphoblastic leukemia (ALL). AML patients were in molecular CR after induction/consolidation therapy and had tumor-free autografts whereas the ALL patient who remained bcr-abl (p190) positive after chemotherapy showed molecularly detectable disease in BM harvest although quantitative analysis did not demonstrate a higher number of copies of the transcript (data not shown).

**Engraftment Results**

All patients submitted to BM harvest proceeded to autologous transplant at a median of 2 months (range 1-6) from stem cell collection. None of the 8 patients with inadequate PBSC collection (i.e. less than 1x10^6 CD34+ cells/Kg) were reinfused with peripheral blood cells along with G-CSF-primed BM. Engraftment data after high dose chemotherapy are shown in Table 3 and Fig.1. Patients are categorized according to diagnosis since the hematopoietic recovery of leukemic patients was significantly slower than that of patients with lymphoproliferative disorders. Six patients who died in the peritransplant period were excluded from analysis (see below). The median times to neutrophil engraftment were 23 and 13 days (p < .00001) for leukemia and lymphoma/myeloma patients, respectively (Fig. 1a). According to the faster neutrophil recovery, the percentage of lymphoma/myeloma patients with documented infections and submitted to
intravenous antibiotics treatment was significantly lower (both p values were < 0.05) than that of leukemia patients.

The median times to an unsupported platelet count of 20 and 50x10^9/L were 52 and 90 days and 15 and 22 days for leukemia and lymphoma/myeloma patients, respectively (both p values < .00001) (Fig. 1b). Two AML patients did not achieve platelet transfusion independence at the time of the last follow up (day +90 from transplant). No correlation was found between the number of CD34^+ cells reinfused and time to neutrophil and platelet engraftment. This finding was also confirmed when we analyzed separately the two groups of patients (data not shown). Furthermore, no difference of engraftment was observed between patients receiving more or less than 0.7 x 10^6 CD34^+ cells/Kg (i.e. the median number of progenitors infused in our patient population). Median times of hospitalization after autograft were 27 and 17 days for leukemia and lymphoma/myeloma individuals, respectively (p < 0.01). No patients were readmitted into hospital after discharge due to late infections.

TRM and overall survival after autologous transplant

Nineteen patients (22.1%) have died so far. Six patients (acute leukemia =3; lymphoma/myeloma =3; 7%) died within 40 days from autologous transplant: four were procedure-related deaths (pulmonary edema =1, the day of BM reinfusion; sepsis =3, at days +12, +14 and +31 from autograft) (4.65%) whereas 2 leukemic patients died following early relapse (=1, at day +35) or progression (=1, day +25) of the disease. Thirteen additional deaths occurred during follow up due to recurrence/progression of the disease. With a median follow up for the study population of 24.5 months, the overall survival at 36 months of lymphoma/myeloma and leukemic patients is 77% and 62%, respectively (Fig.2).
DISCUSSION

Randomized studies have demonstrated that G-CSF-primed BM supports hematopoietic recovery after high-dose chemotherapy recovery as rapidly as G-CSF-mobilized PBSC (15, 16) and is more effective than unprimed BM (15). Fast BM reconstitution after transplant occurs despite the slight increase, if any, of the stem/progenitor cells content of cell harvests as compared with steady-state collections (15). To explain this apparent discrepancy, we previously demonstrated that G-CSF exerts a “priming effect” on BM cells by enhancing the cycling of hematopoietic progenitors and by increasing the response of BM cells to subsequent treatments (in vitro and in vivo) with cytokines (31). Despite similar engraftment data, PB is, by far, the most utilized source of autologous stem cells to support BM function after myeloablative chemoradiotherapy. However, there is significative proportion of cancer patients, ranging from 10 to 30% (1), who are either poor mobilizers or non-mobilizers at all. For these patients, there is as yet no standard procedure for stem cell collection. Unprimed back-up marrow frequently results in delayed platelet recovery (24, 32) and is associated with a high TRM (6), whereas a second mobilization course has been successful in only 48% of patients who did not collect > 2.5 X 10^6 CD34+ cells/Kg with the first attempt (33). A more promising approach relies on the use of high doses of G-CSF, or the combination of G-CSF and GM-CSF, which successfully mobilized, in small series, the majority of patients who had an insufficient cell yield during the first mobilization strategy (34-36). On the other hand, the mobilization potential of newer agents such as stem cell factor, FLT3-ligand, thrombopoietin, IL-8 and their combinations remains to be fully clarified in the clinical setting.

The number of circulating CD34+ cells during PBSC mobilization is the conventional criteria for starting leukaphereses. However, no generally agreed threshold exists to commence PBSC collection. Twenty cells/µL is the minimum peak concentration of CD34+ cells that many transplant centers have establish to start leukaphereses (1). In addition, 1 to 2 x 10^6 CD34+ cells/Kg is the minimum number of PBSC to reinfuse to obtain a rapid neutrophil recovery (1, 6, 7). In this study we considered poor mobilizers patients with less than 10 CD34+ cells/µL (24, 25) and they were...
submitted to G-CSF-primed BM harvest. Similarly, BM harvest was offered to patients whose PBSC collection contained less than $1 \times 10^6$ CD34$^+$ cells/Kg. By considering that autologous stem cell transplantation has proven to be the best therapeutic option for relapsed/refractory lymphoma (37, 38) and multiple myeloma patients (39), it appears to be crucial to develop strategies to bring to transplant as many individuals as possible.

In our Institutions, from February 1995 to December 2002, 86 consecutive patients with hematological malignancies met these criteria and were enrolled in a prospective non-randomized study. The study was designed to assess the hematopoietic recovery, the TRM and all the clinical parameters correlated with effective BM reconstitution after reinfusion of G-CSF-primed BM to support high-dose chemotherapy. It should be noted that all patients entered in our study and submitted to BM harvest were subsequently transplanted.

Our results demonstrated the feasibility of BM harvest in cancer patients non mobilizing PBSC who had been primed for 3 days with G-CSF. The content of CFU-C and CD34$^+$ cells was superimposable to that of previously reported lymphoma patients who were not tested for their capacity to mobilize PBSC (15). When reinfused, these cells engrafted rather rapidly and the results compare favourably with those observed with unprimed BM. In fact, our previous experience of autologous transplantation for AML patients in first CR conditioned with busulphan and cyclophosphamide, showed a median of 25 and 36 days to neutrophil recovery and 87.4 and 150 days to platelet transfusion independence for patients reinfused with both BM and PBSC (30) or BM alone (29), respectively. However, it should be noted that in earlier studies (29, 30), post-transplant hematopoietic growth factors were administered, upon clinical indication, in only 45% of the patients. Similarly, relapsed or refractory lymphoma patients who were transplanted with BM cells after BAVC or BEAM preparative regimens recovered an ANC > $0.5 \times 10^9$/L in a median of 14 and 11 days and a PLT count > $20 \times 10^9$/L in 20 and 15 days according to whether they received G-CSF or G-CSF/IL-3 combination after stem cell reinfusion (26). Notably, reinfusion of primed-BM did not result in delayed PLT recovery as compared to our historical controls. This is an
important finding since transplantation of low numbers of PB mobilized CD34+ cells (i.e. < 2 x 10^6/Kg) has been associated with slow PLT reconstitution. Moreover, almost all patients enrolled in this study (including leukemia patients), were given G-CSF after transplant, which may negatively impact on PLT recovery. However, the PLT recovery of study patients appears to be slower than that of leukemia (29) and lymphoma/myeloma (29 and data not shown) patients reinfused with PBSC in the same period of time.

Interestingly, we did not find a correlation between the number of CD34+ cells reinfused and hematopoietic engraftment and we could not set a threshold value predictive of a rapid engraftment. This was also true when the two groups of study patients were analyzed separately. Thus, the speed of recovery of BM function may be mainly due to the underlying disease and the conditioning regimen. However, previous studies have demonstrated that specific CD34+ cell subsets, which were not evaluated in the present study, are more reliable predictors of fast engraftment than total CD34+ cells (40-42). The TRM rate in our series (which includes 24.4% of leukemic patients) was 4.65%, which is in the range of what is commonly observed after autologous stem cell transplantation for heavily pretreated patients. No late deaths (beyond day +40) due to infection were observed in the follow up. As a result, the overall survival of study patients (Fig. 2) was comparable to that of our historical controls (26, 29, 30) and appears to be better than that of poor mobilizers transplanted with unprimed BM (6).

The good engraftment in our patients rescued with primed-BM indicates that failure of PBSC mobilization is not always due to poor marrow quality. Conversely, a specific impairment of mobilization, in the presence of adequate marrow may occur. In this regard, the better understanding of the mechanisms of mobilization may contribute to the development of more effective protocols for true “non-mobilizers”. An interesting approach for such patients may include the combination of G-CSF and the growth hormone (43).
In conclusion, we demonstrate that G-CSF-primed BM induces sustained and multilineage hematopoietic recovery after myeloablative chemotherapy and represents an effective source of stem cell for cancer patients eligible for autologous transplant.
REFERENCES


FIGURE LEGENDS

Fig.1  **Hematopoietic recovery after myeloablative chemotherapy and reinfusion of G-CSF-primed BM.** Kaplan-Meier plot of probability of recovery of neutrophils to $0.5 \times 10^9/L$ (A) and recovery to an unsupported platelet count of $20 \times 10^9/L$ (B) in lymphoma/myeloma (LY/MM) and acute leukemia (AL) patients. As expected, BM reconstitution was significantly slower in leukemia patients.

Fig.2  **Overall survival of patients submitted to autologous BM transplantation.** Probability of survival for lymphoma/myeloma (LY/MM) and acute leukemia (AL) patients undergoing reinfusion of autologous primed-BM to support high-dose chemotherapy.
### Table 1. Study Patients

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Abbreviations: CHT, chemotherapy; RT, radiotherapy.° Indolent lymphoma (=10); aggressive lymphoma (=31). * All patients had stage III A disease according to Durie and Salmon classification. §Fourteen AML patients were in first CR. For further details see the text.
Table 2. BM harvest and stem cell reinfusion

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Abbreviations: CFU-C, colony forming-unit cells.° Data available on 23 patients. * data available on 52 patients.
### Table 3. Engraftment data

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<td>% DOCUMENTED INFECTIONS</td>
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<td>57.1§</td>
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<td>DAYS</td>
<td>11</td>
<td>7 – 25</td>
<td>7</td>
<td>4 – 32</td>
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<td>DAYS ON G-CSF AFTER ABMT **</td>
<td>11</td>
<td>2 – 40</td>
<td>11</td>
<td>5 – 35</td>
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<tr>
<td>DAYS TO HOSPITAL DISCHARGE</td>
<td>27§</td>
<td>14 – 39</td>
<td>17</td>
<td>12 – 40</td>
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Abbreviations: ANC, absolute neutrophil count; PLT, platelet count. * Six patients are not evaluable for hematopoietic reconstitution and 2 additional patients are still platelet transfusion dependent. For further details see the text. ** All lymphoma/myeloma patients received 5µg/Kg/day of G-CSF starting day +6 post autograft. Eighteen/21 acute leukemia patients received G-CSF upon clinical indication. § p values were < 0.05.
Fig. 1
Fig. 1
Autologous transplantation of granulocyte colony-stimulating factor-primed bone marrow is effective to support myeloablative chemotherapy in patients with hematological malignancies and poor peripheral blood stem cell mobilization

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