

variables. Cox proportional hazards model was used to identify risk factors for survival. Analyzed risk factors were: age, sex, diagnosis, disease stage, acute GVHD (grade II-IV), extensive c-GVHD, stem cell source (cord blood x bone marrow), use of antibodies directed to T-cells and HLA matching. Diagnosis were: CML-46; AML/MDS-40, ALL-34, OTHERS-5. Male: 78; female: 44; median age 17 years (range: 1-55). Cell source was bone marrow in 95 patients, cord blood in 30 patients. Conditioning regimen was nonmyeloablative in 8 patients and conventional in 114 patients. 25 patients received ATG or ALG as part of their conditioning regimen and 90 patients received cyclophosphamide and TBI. Sixty-six patients (53%) had advanced disease at the time of transplant (CML advanced phase, AML or ALL in > second remission, relapsed or refractory).

**RESULTS:** Acute GVHD grade II-IV was observed in 51 patients (41%) and was the primary cause of death in 9% of the patients. Extensive chronic GVHD was observed in 32 patients (26%) and was the primary cause of death in 13% of the patients. Other causes of death included: infection in 32 (41%) and relapse in 21 (27%) of the patients. Estimated 10 years overall survival was 40% with a median survival of 189 days. There was no difference in survival according sex, diagnosis, stem cell source, type of conditioning, number of cells infused or HLA compatibility. There was a significant better 10 years survival for early disease, compared to advanced disease (55% x 20%;  $p=0.0005$ ), age less than 18 x more than 18 (60% x 20%;  $p=0.0012$ ). Extensive c-GVHD was protective for overall survival ( $P=0.0340$ ; Odds ratio =0.3998; 95% CI=0.1758 to 0.9092).

**CONCLUSIONS:** 1) Estimated 10 y overall survival was 55% for patients with early disease; 2) Extensive c-GVHD had a protective effect on OS, probably due to graft versus malignant effect. 3) Age less than 18 years and early disease were favorable risk factors for survival.

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### PLATEAU IN THE DISEASE-FREE SURVIVAL CURVE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION IN PATIENTS WITH ACUTE MYELOID LEUKEMIA MAY SIGNIFY CURE: A LONG-TERM SINGLE INSTITUTION EXPERIENCE

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**Introduction:** Allogeneic Stem Cell Transplantation (AlloSCT) through the graft-versus-leukemia (GVL) effect holds the promise of a long-term cure in patients with acute myeloid leukemia (AML).

**Methods:** In an attempt to examine whether AlloSCT provides long-term disease control in patients with AML, we retrospectively evaluated our experience and analyzed the outcomes of ASCT in patients with AML from 1978 to 2005.

**Results:** Fifty-nine males and 46 females (n=105) of median age 32 years (range: 5-60 years) were treated. Of these, 65 were in CR at the time of transplantation, 40 patients were transplanted with active disease. Fifty patients were transplanted in first remission. Bone marrow was used in 75 patients as the source of stem cells prior to 1995 and peripheral blood stem cells (PBSC) were used in 30 patients. Ninety-four of 105 patients engrafted (90%). Median time for neutrophil recovery was 16 days (range: 9-90 days) and 23 days (range: 9-106 days) for platelets. Median duration of follow-up for those who did not succumb to early transplant-related mortality (<100 days) was 2 years (range: 102 days-21 years). Median survival time of this cohort was 2 years. Of the 105 patients, 77 have died. Thirty-four patients (32%) died within 100-days of transplantation. Overall survival (OS) of all patients who did not succumb to TRM was 47% at 5-years, 38% at 10-years and 15-years respectively. No relapse occurred after 4.25 years. OS in patients transplanted in CR (n=65) at 5-years was 72%, and at 10 and 15-years was 62% respectively. For those transplanted with disease (n=40), a complete response was achieved in 23 patients (22%), with a median survival of 214 days. Disease status at transplantation was a significant variable for survival ( $p<0.01$ ). Most frequent cause of death was infection (27

out of 105 patients). Five patients developed late onset myelodysplastic syndrome/secondary malignancy. Patients with any graft-versus-host-disease (GVHD) had better survival compared to patients with no GVHD, underscoring the role of GVL effect in long-term disease control.

**Conclusion:** In conclusion, AlloSCT provides a possible cure in a proportion of patients with AML as evidenced by a plateau in the DFS curve after 4.25 years.

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### REDUCED-INTENSITY STEM CELL TRANSPLANTATION IN PATIENTS WITH HIGH-RISK ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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**Introduction:** Despite the optimal use of the antileukemic agents, reported cure rates do not exceed 40% in high-risk ALL adult patients. The use of hematopoietic stem cell transplantation (HSCT) is another option in these patients and non-myeloablative conditioning is a friendly alternative to the conventional and more toxic myeloablative radio-chemotherapy scheme, but there is very limited information using this kind of transplantation in ALL. We prospectively evaluated the therapeutic value of non-myeloablative conditioning HSCT in 43 high risk ALL patients in second or subsequent remission. **Patients and methods.** Forty three ALL high-risk patients were prospectively allografted, using HLA-identical siblings as donors. Patients received oral busulphan 4 mg / Kg/2 days, i.v. cyclophosphamide 350 mg /m<sup>2</sup>/3 days and i.v. fludarabine 30 mg /m<sup>2</sup>/3 days; oral cyclosporin A 4 mg / Kg was started on day - 1 and i.v. methotrexate 5 mg / m<sup>2</sup> was delivered on days + 1, + 3, + 5 and + 11. Median age of the patients was 19 years; there were 19 females. Patients received a median of  $5.0 \times 10^6$  / Kg CD34 cells. **Results:** Median time to achieve above  $0.5 \times 10^9$ /L granulocytes was 14 days, whereas median time to achieve above  $20 \times 10^9$ /L platelets was 15 days. Thirteen patients (30%) are alive 491 days (median) after the HSCT. The 861-day probability of survival is 22%, whereas median survival is 200 days. Ten patients (23%) developed acute graft versus-host disease (GVHD), and 8 patients (18.6%) developed chronic GVHD. Twenty eight (65%) patients showed relapse, in 9 cases despite the GVHD. Thirty patients died between day 47 and 1050 after the HSCT, most of them (70%) of an ALL relapse. The 100-day mortality was 25.5%. **Conclusion:** Relapse remains the first cause of death in high-risk ALL patients. Non-myeloablative HSCT seems to have limited therapeutic effect in ALL patients with advanced disease. New ideas and emerging strategies should be employed in order to improve the outcome of these patients, like enhancement of graft-versus leukemia effects and the use HSCT in first complete remission.

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### NEUROLOGICAL COMPLICATIONS IN THE RECIPIENTS OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT

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The prevalence of neurological complications in allogeneic hematopoietic cell transplant (AlloHCT) recipients, the mechanisms of its development, and its impact on outcome are not well defined. We reviewed the medical records of 302 consecutive patients, who underwent AlloHCT for hematologic diseases at Princess Margaret Hospital between January 2002 and November 2005. Patient, disease and transplant related factors were systematically analyzed. Stem cells were obtained via peripheral blood (n=213) and bone marrow (n=89) from HLA-matched siblings/other family (n=224), HLA-matched unrelated donors (n=52) and HLA-mismatched donors (n=26). Median age of the recipients was 45 years