increased hazard ratio for death; however, a dose above 8
mental increases in CD34 dose were associated with an in-
Prevention of rejection by donor Th2/Tc2.R cells abrogated
Th2/Tc2 cells only partially reduced HVGR (cohort 4
of aGVHD (grades II-IV versus grades 0-I) (p
investigation to optimize disease indications and CD34
doses of both were associated with development of aGVHD (p
0.04). NM conditioning has a role in alloPBSCT and further
controls had increased post-BMT allospecific CD4
reactive CD4
CD8
mechansims. To evaluate whether alloreactive host T cells were
perforin or fasL molecules associated with clonal deletion
progression. After day
phocyte infusion for disease progression. 100-day NRM was
pts developed extensive cGVHD. 14 pts required donor lym-
cGVHD significantly correlated with improved OS (p
follow up of 505 days (range 31-2029). OS at 2 and 3 years was
abilities for overall survival (OS) and progression free survival
(PFS) at one year were 61% and 48%, respectively with median

Ex vivo rapamycin generates murine Th2 cells that potently abrogate GVHD. We thus hypothesized that rapamycin would generate Th2/Tc2 cells (Th2/Tc2.R cells) that prevent fully MHC-disparate hematopoietic stem cell (HSC) rejection. To test this hypothesis, we utilized a model of rejection involving lethal host irradiation and quantitative host T cell addback [see cohorts, Table]. Th2/Tc2.R cells recipients had consistent allo-engraftment (>99% donor, n=9/10; rejection, n=1/10); in con-
tact, contrast Th2/Tc2 recipients had graft rejection (n=9/10)
or mixed chimerism (n=1/10). Post-BMT host-vs-graft re-
sequences (HVGR) were quantified by the following method: (a)
spleen cell harvest and enumeration; (b) 24 h host (syngeneic) or
donor (allogeneic) dendritic cell stimulation; (c) cell-surface
flow cytometry with anti-CD4, anti-CD8 and anti-host antibod-
ies; (d) Miltenyi IFN-gamma cytokine capture flow cytometry;
and (d) calculation of absolute number of host anti-donor allo-
reactive CD4+ and CD8+ T cells per spleen. Grant rejection
controls had increased post-BMT allospecific CD4+ and CD8+ T cells secreting IFN-g (cohort 3>cohort 2; p<.001).
Prevention of rejection by donor Th2/Tc2.R cells abrogated this HVGR (cohort 5<cohort 3; p<.001); in contrast, donor
Th2/Tc2 cells only partially reduced HVGR (cohort 4<cohort 3; p<.05). Cohorts 6, 7, 8, and 9 demonstrated that rapamycin-
generated donor T cells prevented day +28 for CD34+ and day +80 for
CD34+ . aGVHD occurred in 42/60 (70%) pts (grade I in 14 and
grades II-IV in 28), and cGVHD occurred in 28/52 (54%); 12
pts developed extensive cGVHD. 14 pts required donor lympho-

Hyperglycemia during Neutropenia was associated with poor outcome in patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT)

Background
Recipients of allogeneic HSCT frequently require support with parenteral nutrition and immunosuppressive drugs, in expectation of an increased risk of infections associated with hyperglycemia, particularly in the neutropenic period. Previous reports showed that hyperglycemia was associated with morbidity and mortality in ICU (ref van den Verge et al. N Engl J Med. 2001 Nov 8;345(19): 1359-67). There was no previous study which assessed the clinical impact of hyperglycemia in patients undergoing myeloablative HSCT. Patients and Methods
A cohort of 112 consecutive adult patients with hematological malignancies treated between January 2002 and June 2006 was reviewed retrospectively, and 21 patients were excluded due to graft failure, preexisting infectious diseases or preexisting neutropenia. The remaining 91 patients (Age median 35.5, 18-57) were categorized according to
normoglycemia (BG<110 mg/dl, n=28), 2) "mild hyperglycemia" (110<BG<150 mg/dl, n=49) and 3) "moderate and severe hyperglycemia" (150 mg/dl<BG, n=14). Conditioning regimens included BU/CY (n=45), CY/TBI (n=43) and CA/CY/TBI (n=3). GVHD prophylaxis included cyclosporine- (n=62) and tacroli-
mus-based regimens (n=29). Stem cell sources included bone marrow (n=46), peripheral blood (n=41) and cord blood cells (n=4). The primary endpoint of this study was the occurrence of febrile neutropenia (FN) and infection during neutropenia. The secondary endpoints were parameters for organ dysfunction, aGVHD, overall survival (OS) and treatment-related mortality (TRM). Re-
Results There was no significant difference between the 3 groups in the occurrence of FN or documented infection. However, hyperglycemia was significantly associated with organ dysfunction and aGVHD. OS was better and TRM was less in group 1 compared with group 2 and group 3. Conclusion Degrees of hyperglycemia during neutropenia was associated with an increased risk of organ dysfunction and aGVHD, which further led to higher TRM and lower OS. These results support the possibility that intensive glucose control reduces morbidity and mortality after HSCT.

<table>
<thead>
<tr>
<th>blood glucose level</th>
<th>normoglycemia (n=28)</th>
<th>mild hyperglycemia (n=49)</th>
<th>moderate and severe hyperglycemia (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FN</td>
<td>25 (89%)</td>
<td>43 (88%)</td>
<td>13 (93%)</td>
</tr>
<tr>
<td>Documented infection</td>
<td>9 (32%)</td>
<td>10 (20%)</td>
<td>6 (43%)</td>
</tr>
<tr>
<td>hypercreatinemia (serum creatinine ≥2mg/dl or more than twice of baseline)</td>
<td>1 (4%)</td>
<td>4 (8%)</td>
<td>4 (29%)</td>
</tr>
<tr>
<td>hyperbilirubinemia (serum bilirubin ≥2mg/dl)</td>
<td>3 (11%)</td>
<td>11 (22%)</td>
<td>6 (43%)</td>
</tr>
<tr>
<td>CRP elevation (serum CRP ≥15 mg/dl)</td>
<td>4 (14%)</td>
<td>15 (31%)</td>
<td>9 (64%)</td>
</tr>
<tr>
<td>aGVHD (II-IV)</td>
<td>4 (14%)</td>
<td>18 (38%)</td>
<td>7 (58%)</td>
</tr>
<tr>
<td>OS (1-year)</td>
<td>87%</td>
<td>70%</td>
<td>56%</td>
</tr>
<tr>
<td>TRM (1-year)</td>
<td>5%</td>
<td>17%</td>
<td>30%</td>
</tr>
</tbody>
</table>

236 THROMBOTIC MICROANGIOPATHY AFTER HSCT: MUCOSITIS AS A RISK FACTOR FOR SURVIVAL AND HIGH PREVALENCE OF ACUTE GVHD, CMV AND GRAM POSITIVE INFECTIONS

Funke, V.A.M.¹, Oliveira, M.M.¹, Ruiz, J.¹, Bonfim, C.M.¹, Bitencourt, M.A.¹, Coutinho, E.N.¹, Setubal, D.C.¹, Zanis-Neto, J.¹, de Medeiros, C.P.¹, Pasquini, R.¹ *Hospital de Clinicas - Universidade Federal do Paraná, Curitiba, PR, Brazil.

INTRODUCTION: Thrombotic microangiopathy is a rare complication after HSCT. Given the different pathophysiology of the disease and high mortality observed, our purpose is evaluating clinical characteristics of these patients and risk factors for survival.

PATIENTS AND METHODS: From 1991 to 2004, 1066 HSCT were performed at HC-UFPR (Curitiba, Brazil). We identified in our database 17 patients with the diagnosis of thrombotic microangiopathy (prevalence of 1.6%). M:F=4:13, Median age: 11; Diagnosis included: SAA: 2; Fanconi anemia: 4; Acute myeloid leukemia: 7, Others 2.

Conditioning regimen consisted of BUCY in 9/17 (52%); CI + TBI in 3/17 (18%) of the patients. NMA regimens in 18% and others in 12% of the patients. Immune prophylaxis consisted of CSA and MTX in 52% of the patients. Twelve patients received related and five received unrelated donor transplant.

Marow was the stem cell source in all but one patient who received cord blood.

Twelve patients were HLA identical, three patients had a class one mismatch, one patient had a class II mismatch and one patient had more than one mismatch.

Median number of cells infused were 2,57 × 10^8/KG.

RESULTS A-GVHD grade II-IV was present in 12 (70%) patients and extensive C-GVHD was present in only 18% of the patients. Median survival was 99 days and estimated overall survival in 23 years is only 15%, despite therapy. Infection was present in all but one patient (94%). Ten patients had serious bacterial infections (58%), eight of them were gram-positive bacteria. Fungal infection was identified in five patients (2 Candida sp and 3 Aspergillus sp). Viral infection was identified in 12 patients (eight of them with CMV positive antigenemia). Causes of death included: A-GVHD in 4 patients, C-GVHD in 2 patients, infection in 6 patients, bleeding in two patients and persistent disease in one patient. The only significant factor for survival was severe mucositis (more than grade II).

CONCLUSION: 1. OS was extremely low (15%) despite therapy; 2. Infection (especially gram-positive bacterial infections and CMV positive antigenemia) was present at the majority of the patients and was the main cause of death; 3. A-GVHD was present in 52% of the patients; 4. Severe mucositis was associated to a lower survival rate (p=0.02).

237 LONG TERM RESULTS OF ALLOGENIC STEM CELL TRANSPLANT FOR CML IN PEDIATRIC PATIENTS: A STUDY OF 50 CASES TRANSPLANTED OVER 20 YEARS IN A SINGLE INSTITUTION

Funke, V.A.M.¹, Coutinho, E.N.¹, Setubal, D.C.¹, Ruiz, J.¹, Bitencourt, M.A.¹, Oliveira, M.M.¹, Continho, E.N.¹, Zanis-Neto, J.¹, de Medeiros, C.P.¹, Pasquini, R.¹ *Hospital de Clinicas - Universidade Federal do Paraná, Curitiba, PR, Brazil.

Introduction: Chronic myeloid leukemia (CML) accounts for 2-3% of the leukemias in childhood. The only potential curative treatment is allogeneic hematopoietic stem cell transplantation (HSCT), although promising results achieved with imatinib mesylate in adults substantiate its use as a therapeutic alternative for children. The aim of this study is to analyze the outcomes of HSCT in pediatric patients regarding overall survival (OS) and main causes of death.

Materials and methods: Retrospective analysis of children aged 1-17 years, diagnosed with CML who underwent HSCT in a single institution in Brazil between Jan/1984 and Aug/2005. Survival was estimated by Kaplan-Meier curves. Log Rank test was used for comparison of continuous variables.

Results: Fifty patients were assessed, 31 male and 19 female. Median age of 13.5 years (1-17). Forty one patients (82%) were in first chronic phase (CP1) and 9 in advanced phases. The interval between diagnosis and HSCT had a median time of 17.5 months (5-84). The source of stem cells was bone marrow in 44 patients (88%), umbilical cord blood in 5 (10%) and peripheral blood stem cell in 1 (2%). Thirty nine patients (78%) underwent related HSCT and 11 (22%) unrelated donor HSCT. Conditioning regimens: busulfan and cyclophosphamide in 35 patients (70%), 15/40 patients (38%). Fifteen patients (32%) relapsed after HSCT.

Conclusions: 1) Long term follow up of these children with CML who underwent allogeneic HSCT demonstrate an OS of 50%, reaching 70% in low risk patients. 2) Main causes of death were relapse, acute and chronic GVHD.

238 RISK FACTOR ANALYSIS FOR SURVIVAL IN 125 UNRELATED TRANSPLANTS FOR MALIGNANT DISEASES PERFORMED OVER TEN YEARS IN A SINGLE CENTER IN BRAZIL

Funke, V.A.M.¹, Coutinho, E.N.¹, Setubal, D.C.¹, Ruiz, J.¹, Bonfim, C.M.¹, Bitencourt, M.A.¹, Oliveira, M.M.¹, Zanis-Neto, J.¹, de Medeiros, C.P.¹, Pasquini, R.¹ *Hospital de Clinicas - Universidade Federal do Paraná, Curitiba, PR, Brazil.

INTRODUCTION: Unrelated transplants are increasingly used for therapy of malignant diseases. The objective of this study is evaluating risk factors for overall survival among 125 unrelated transplants performed at the BMT center of HC-UFPR in Curitiba, Brazil.

PATIENTS AND METHODS: We analyzed results of unrelated HSCT performed from 07/95 to 06/05. Kaplan-Meier was used to estimate overall survival. Log rank test was used to compare survival curves and Fisher’s exact test for comparison of categorical