**Patients and Methods:** Between 10/04 and 6/06, 24 patients (pts) with high risk/relapsed/refractory hematologic malignancies have undergone NST using a modification of our original Pt-TBI regimen. The median age was 60 years. The median number of prior therapies was 2 (range 0-6). Diseases transplanted included acute lymphoblastic leukemia (n=3), myelodysplastic syndrome (n=2), acute myelogenous leukemia (n=8), chronic lymphocytic leukemia (n=3), indolent non-Hodgkin's lymphoma (n=2), and mantle cell lymphoma (n=6). Conditioning consisted of Pentostatin 4 mg/m2 daily on day -10, -9, and -8, followed by 200 cGy TBI on day -1. Post-grafting immunosuppression consisted of cyclosporine/mycophenolate mofetil. **Results:** Transplantation was performed using mobilized progenitor cells from matched related (n=8) or unrelated (n=16) donors. Death prior to 100 days post transplant occurred in 4 unrelated donor transplants. The median nadir values for hemoglobin, neutrophil count and platelet count were 8.9 g/dl (range 7.6-13.7), 300/mm$^3$ (range 0-1900), and 63/mm$^3$ (range 9-165) respectively. Primary graft failure/autologous recovery occurred in one patient with mantle cell lymphoma. The median values for CD3+ cells and WBC at day 28 were 85% and 90% donor cells respectively. The analogous median values at day 70 were 85% and 100% respectively. One pt with a myelproliferative disorder and thalidomide as his only prior therapy experienced late graft failure despite donor lymphocyte infusions. The cumulative incidence of grade II-IV acute graft-versus-host disease was approximately 54% (14% in related versus 68% in unrelated donors, P=0.08). The probability of extensive chronic graft-versus-host disease in patients surviving beyond 100 days is 38%. The cumulative incidence of relapse at one year post transplant is 43%. The one year probabilities of event-free and overall survival are 41% and 61% respectively. **Conclusions:** This modification of our original Pt-TBI regimen continues to demonstrate fairly minimal regimen related toxicity, although as expected hematologic toxicity appears to be more significant than with our prior day -21 Pentostatin regimen. Graft versus host disease continues to be a major cause of morbidity/mortality, particularly in unrelated donor transplants. Further studies will concentrate on attempting to decrease the incidence of acute and chronic graft versus host disease through the use of T-cell depletion with in vitro alemtuzumab.

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### UMBILICAL CORD BLOOD TRANSPLANTATION FOR ADULT PATIENTS WITH CHRONIC MYELOID LEUKEMIA

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Chronic myelogenous leukemia (CML) was primarily treated with HSCT until imatinib mesilate was shown to be effective and safe for patients with early chronic phase CML. However, patients who fail imatinib therapy due to disease progression or drug intolerance still require HSCT. Umbilical cord blood (UCB) has been an increasingly used source of hematopoietic stem cells for transplantation (HSCT) of patients with hematologic malignancies who lack a suitable sibling donor. We report here on 20 adult patients who underwent UCB transplantation (UCBT) for Ph+ CML at the University of Minnesota between 1998 and 2005. Patient received myeloablative (MA, n=12) or nonmyeloablative (NMA, n=8) conditioning, The median age was 46 y (r: 18-58), 12 (60%) were male, and median weight was 78 kg (r: 57-103), and 13 (65%) were CMV positive. The MA conditioning was Bu/Cy (n=2) Cy/TBI ± ATG (n=4), or Cy/Fludarabine(Flu)/TBI (n=6). The NMA conditioning was Bu/Flu/TBI (n=2) or Cy/Flu/TBI± ATG (n=6). Posttransplantation immunosuppression was CsA alone (n=1), CsA/methylprednisolone(MP) (n=5), or CsA/MMF (n=14). Eleven patients (55%) receive a double UCB graft. The highest HLA disparity of UCB units was 4/6 (n=13), 5/6 (n=5), and 6/6 (n=2). Six patients (30%) were in first chronic phase (CP1) and 14 (70%) were in accelerated phase (AP) CML. The median TNC dose infused was 2.9 × 107/kg (r:1.2-5.3) and median CD34 dose infused was 4.8 × 105/kg (r: 0.7-12.7). The median time from diagnosis to transplant was 24.5 months (r: 6.7-118.8), and the median follow-up of surviving patients was 2.9 yrs (r: 0.7-.7.0). There were no failures of neutrophil engraftment. In the MA setting median time to neutrophil engraftment was 21d (r:13-33), grade II-IV acute GVHD was 58% (95%CI, 28-88%), 1-yr transplant related mortality (TRM) 41% (95%CI, 13-69), 2-yr relapse rate 10% (95%CI, 0-26), and overall survival 58% (95%CI, 30-86). In the NMA setting median time to neutrophil engraftment was 13d (r:5-32), grade II-IV acute GVHD was 63% (95%CI, 28-98%), 1-yr transplant related mortality (TRM) 38% (95%CI, 6-70), 2-yr relapse rate 13% (95%CI, 0-34), and overall survival 50% (95%CI, 15-85). There was no statistically significant difference between MA and NMA conditioning regimens on all outcomes. In this report we show that UCB appears to be a safe and effective HSC for transplantation of patients with CML.

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### FLUDARABINE/FULL DOSE I.V. BUSULFAN CONDITIONING REGIMEN IN ALLOGENEIC PBSC TRANSPLANTATION FOR HIGH RISK PATIENTS

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Fludarabine/ full dose busulfan (FluBu) conditioning regimen causes moderate extrahematologic toxicity and low rates of acute graft-versus-host disease (GVHD) in allogeneic hematopoietic stem cell transplantation (HSCT).

In this study we utilized this regimen in 21 adult patients with hematologic malignancies, including 15 patients (71%) at high risk of relapse (8 acute leukemia in relapse, 3 NHL in relapse, 1 NHL in CR2, 1 myelofibrosis in transformation, 2 CML-AP resistant to imatinib) and 6 patients at standard risk (3 AML in CR1, 2 CML-CP resistant to imatinib, 1 MDS). All patients were prepared with fludarabine (30 or 40 mg/m$^2$/day) for 4 days from d-9 to d-6 and i.v. busulfan (3.2 mg/kg/day) for 4 days from d-5 to d-2, and received an HLA matched related (n=14) or unrelated (n=7) peripheral blood stem cell (PBSC) transplant. Mean number of CD34+ cells infused was 7.3±4.0 × 10$^6$/kg. Thymoglobulin was added to the preparative regimen on d -3 to d-1 in 9 patients, including those receiving an unrelated HSCT. Acute GVHD prophylaxis included standard tacrolimus and methotrexate on d1, d3, d6 and d11. All patients fully engrafted but one ALL patient transplanted in relapse who recovered with leukemic blasts. Median times to ANC 0.5×10$^9$/L and platelet 20×10$^9$/L were 15d (range: 18-24) and 13d (range: 0-24), respectively. Acute GVHD grade II-IV was observed in 24% of the patients (grade III-IV 18%) and chronic GVHD in 9 of 14 evaluable patients (64%). Of 21 patients, 8 died in full relapse with bacterial or fungal infection and 2 for acute GVHD grade III and fungal infection. Median time to relapse after HSCT was 72d (range: 18-328). At a median follow-up of 447 d (range: 120-1196) for patients who are alive, the overall survival (OS) and event-free survival (EFS) are 52% and 48%, respectively. In the group at high risk the OS and EFS are both 33% at 447 d median follow-up (range: 147-834).

FluBu conditioning regimen, besides causing low transplant-related morbidity and mortality, is also effective in high risk patients receiving an allogeneic PBSC transplant from related or unrelated donors.

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### HAPLOIDENTICAL NON-MYELOABLATIVE HEMATOPOIETIC TRANSPLANT WITH SIROLIMUS BASED IMMUNOSUPPRESSION YIELDS RELIABLE ENGRAFTMENT AND MAY RESULT IN LONG TERM SURVIVAL

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Timely availability of matched donors limits allo-hematopoietic transplant (HCT) options for many otherwise suitable patients. We have explored sirolimus (rapamycin) based immuno-