cGVHD. 12 pts have relapsed at a median of 128 days (range 76-512) post transplant with a one year actuarial OS of 65%. **Conclusion:** This approach permits accurate delivery of a targeted systemic exposure to IV busulfan, is well-tolerated, and will allow additional dose escalation. Relapse, as opposed to toxicity, remains the major challenge.

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TREOSULFAN: AN ATTRACTIVE ALTERNATIVE IN THE CONDITIONING IN BONE MARROW TRANSPLANT FOR THALASSEMIA

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Traditionally Busulfan and Cyclofosfamide are used with or without serotherapy in the conditioning for beta thalassemia. Due to a high rejection rate in our institution, Melfalan has been added resulting in a marked reduction of rejection. Toxicity of this regimen is tolerable and consists mainly of mucositis and occasionally of VOD.

Treosulfan is an alkylating agent with a supposedly lower toxicity profile than other alkylating agents.

In 12 previously treated thalassemia patients (class 2-3) conditioned with Busulfan, Melfalan, Cyclofosfamide and serotherapy, mucositis WHO grade 1-2 was seen in 2 patients and grade 3– 4 in 9 patients. VOD was seen in 4 patients and 2 patients had mild VOD. One patient died due to MOF. Acute GVHD was seen in 6 patients. Chronic GVHD (mild) in 2 patients. Two patients rejected but were successfully retransplanted. Ten patients had full donor chimerism, two patients showed stable mixed chimerism.

In comparison the results in 5 beta thalassemia patients (class 2-3) conditioned with Treosulfan 10 -14 mg/m2, Cyclofosfamide 120 mg/kg, Melfalan 140 mg/m2 with additional serotherapy (either ATG or Campath). Two patients had a matched unrelated donor, 3 patients had identical related donors. Three patients received Treosulfan 10 mg/m2. One patient rejected early and was successfully retransplanted with Treosulfan 14 mg/m2. The remaining two patients received Treosulfan 14 mg/m2. Engraftment was in normal range. No acute or chronic GVHD was seen. Mucositis was limited in 3 (WHO grade 2) and moderate to severe (WHO grade 3-4) in 2 patients. No VOD was seen. Chimerism was stable mixed in 2 and full donor in three.**Conclusion:** Treosulfan 14 mg/m2 is well tolerated in thalassemia bone marrow transplant patients and shows a lower toxicity profile than busulfan.

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IMPACTS OF COMORBIDITIES ON OUTCOMES OF PATIENTS (PTS) YOUNGER THAN 60 YEARS OLD, DIAGNOSED WITH INDOLENT MALIGNANCIES AND TREATED WITH ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT): A MODEL FOR PTS WITH AUTOIMMUNE DISEASES

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The NIH has stated the growing need to explore the therapeutic and curative potential of allogeneic HCT for autoimmune diseases (BBMT 2005, 11:862). The safety of HCT in pts with significant comorbidities is of a concern. Here, we analyzed whether the HCT-CI, a sensitive tool to capture comorbidities (Blood 2005, 106:2912), could assess how young (<60 year old) pts with indolent malignancies tolerated allogeneic HCT strategies as a hypothetical model for pts with autoimmune diseases. A majority of pts received myeloablative (MA) conditioning (n=364) with cyclophosphamide plus busulfan (79%) or 12 Gy TBI (21%), while a small group of pts (n=79) received nonmyeloablative (NMA)-conditioning with 2 Gy total body irradiation (18%) ± 90 mg/m^2 of fludarabine (82%). Diagnoses were acute myeloid leukemia in 1st remission (27%), chronic myeloid leukemia-chronic phase (40%), myelodysplasia-refractory anemia (16%), chronic lymphocytic leukemia (8%), low grade non-Hodgkin lymphoma (4%), and others (5%). At HCT, NMA-pts differed from MA-pts with respect to age (median 52 vs 41 years,), prior high-dose HCT (9% vs 1%), unrelated grafts (42% vs 31%), and G-PBMC as stem cell source (87% vs 49%). HCT-CI scores of 1-2 and ≥3 were found among 33% and 35% of NMA vs 35% and 17% of MA-pts, respectively. The most frequent comorbidities were pulmonary (24%) and hepatic (16%). After HCT, 4-year cumulative incidences of non-relapse mortality (NRM) were 10%, 17%, and 36% for MA-pts with HCT-CI scores of 0, 1-2, and ≥3, respectively. Proportional hazards models; adjusted for stem cell source, pt age, donor type, and diagnoses, were used to estimate hazard ratios (HR) for NRM and survival. MA-pts with HCT-CI scores of 1-2 or ≥3 had higher adjusted HRs for NRM (1.85, p=0.06 and 4.56, p<0.0001) and all-cause mortality (2.15, p=0.003 and 4.59, p<0.0001) compared to pts with HCT-CI scores of 0. There were no statistically significant differences in NRM between NMA and MA-pts with HCT-CI scores of 0, 1-2, or ≥3 (p=0.7, p=0.1, p=0.18, respectively); however, the small numbers of pts receiving NMA conditioning in each stratum limited the power of these comparisons. We conclude that among young pts with indolent malignancies, NRM and survival are strongly associated with comorbidity after MA-HCT. Therefore, MA-HCT for treatment of autoimmune diseases might be contraindicated for pts with HCT-CI scores of ≥3. Additional data are needed to clarify the usefulness of NMA-HCT in indolent diseases.

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OUTCOME OF PATIENTS ACCORDING TO ETHNIC GROUPS RECEIVING ALLOGENEIC STEM CELL TRANSPLANTATION IN MALAYSIA

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A total of 106 patients received an allogeneic stem cell transplantation at Kuala Lumpur Hospital between 5/1999 and 5/2006. Majority received G-CSF stimulated bone marrow as stem cell source while 20% received PBSC. The race distribution were 52% Malays, 31% Chinese, 9% Indians and 9% other races. The median time to neutrophil engraftment was 19 days and platelet engraftment was 18 days. There was no difference in engraftment days of platelets and neutrophils between G-CSF stimulated marrow and PBSC. The overall survival OS was 61%, event-free survival EFS was 54% and the 100-day transplant mortality rate TRM was 16%. The cumulative relapse rate was 24% and the graft-vs-host disease GVHD rate was 32%.

The overall survival rate according to race was 62% in Malays, 68% in Chinese and 50% in Indians. The cause for mortality in the Malay race was GVHD at 52%, relapse 29% and infection 29%. Amongst the Chinese, the major cause for mortality was relapse 60%, GVHD 20% and infection 10%. In the other races, the cause of mortality was relapse in 70% and GVHD in 20%.

The incidence of moderate Grade II and severe Grade III-IV acute GVHD was 40% and 29% in the Malays, 43% and 10% in the Chinese and 22% and 22% in the Indians respectively. Similarly the incidence of limited and extensive chronic GVHD was 12% and 34% in the Malays, 21% and 18% in the Chinese and 0% and 38% in the Indians.

It is evident that the incidence of severe acute GVHD and extensive chronic GVHD is higher in the Malays than the other races. Severe GVHD was also the major cause of mortality amongst the Malays than the other races. However the rate of relapse was inversely lower in the Malays than in the Chinese and Indians.

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ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN IMATINIB ERA: A SINGLE CENTER COMPARATIVE ANALYSIS OF IMATINIB RECEIVING PATIENTS TO IMATINIB NAIVE PATIENTS

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