karyotype, with most commonly a complex karyotype (37%). Sixteen patients received hematopoietic stem cell transplantation (HSCT) in first remission (n=9) or with active disease (n=7) following a myeloablative (n=10) or reduced intensity (n=6) conditioning regimen. The median survival from the time of diagnosis was 19 months (range, 1 – 82 months). On univariate analysis, complete response to induction therapy was a significant predictor of survival (65% vs. 9%, P < .001). Additionally, there was a trend toward better overall survival for patients who received HSCT compared with the patients who were treated with chemotherapy alone (60% versus 35%, P = .083). Differences in immunophenotypic subtypes or karyotype did not impact the overall survival.

Patients with MPAL represent a rare and heterogeneous category of leukemia with poor prognosis. The stricter classification schema should help to lessen heterogeneity and allow for better understanding of the leukemia, and ultimately better patient outcomes. Our small series suggests that response to induction portends better survival. Furthermore, hematopoietic stem cell transplantation can further improve outcomes.

Long-Term Outcomes of Hematopoietic Stem Cell Transplantation in Pediatric Patients with Acute Leukemia Based on Conditioning Regimen without Total Body Irradiation

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Background: The current acceptable conditioning regimen used for hematopoietic stem cell transplantation (HSCT) in pediatric leukemia consists of total body irradiation (TBI) especially in acute lymphoblastic leukemia (ALL). Considering the complications and limitations of TBI-based conditioning regimens, some studies tried to use non-TBI conditioning regimens.

Methods: From 1992 to 2012 in a retrospective study from our center pediatric patients (age <15) with acute myeloblastic leukemia (AML) and ALL candidate for HSCT included. The patients were prepared using a non-radiation-based conditioning regimen (busulfan/cyclophosphamide in allogenic and busulfan/etoposide in autologous). In the allogenic HSCT, Cyclosporine A and methotrexate were used as graft-versus-host disease (GVHD) prophylaxis regimen.

Results: Of 268 patients with AML (autologous=57, allogenic=104) and ALL (allogenic=107), 137(51%) of them were boys and 131(49%) were girls. The median age at transplantation were 11 years (range: 1-15years) in AML patients and 12 years (range: 0.8-15years) in ALL patients. With a median follow up of 31 months for AML patients, overall survival (OS), disease free survival (DFS) for autologous and allogeneic transplantations were 64%, 59.2% and 69%, 61.5% respectively. In ALL patients with a median follow up of 14 months, OS and DFS were 80.3% and 70%. The most common cause of deaths in both AML and ALL patients was relapse (63% and 71%). Regarding GVHD occurrence, in AML and ALL patients 67 (41.6%) and 61 (57%) did experience acute GVHD. Considering chronic GVHD for AML and ALL patients, results were 20(12.4%) and 13(12.1%).

Conclusion: Regarding the adverse effects of using TBI-based conditioning regimen, it seems that in pediatric patients with AML and ALL using a non-TBI based conditioning regimen can be a good alternative in HSCT. However, large controlled well-designed studies are needed for further understanding of differences between TBI and non-TBI conditioning regimens.
Methods: A retrospective review of the patients who relapsed following an allogeneic HCT for a myeloid malignancy at Mayo Clinic in Arizona was performed. The BM sample closest in time prior to relapse was identified and the morphologic, flow cytometric, karyotypic, FISH, PCR and chimerism results were reviewed.

Results: Out of 187 patients with a myeloid malignancy, 40 (31 AML, 4 MPN blast crisis, 4 MDS, 1 CML) relapsed at a median of 113 days (range 22-820 days) after HCT. Thirty percent of the relapses occurred after a myeloablative HCT. Donor type was equally distributed between matched related and mismatched/matched unrelated donors. A cytogenetic and molecular marker with the diagnosis was identifiable in 22/40 and 6/40 patients respectively. 18/40 patients had residual disease present at HCT. 13/40 patients showed an early relapse within the first 90 days. In the remaining patients, time between the last BM and relapse ranged from 38-184 days (median 69). Abnormal results were found only in 9/27 patients in the preceding BM and included abnormal cytogenetic clone identical to diagnosis in 2 patients; abnormal RT-PCR for BCR/ABL in 1, cytogenetic abnormality in donor cell line in 3, and decreased chimerisms in unsorted marrow cells in 3 patients.

Conclusions: A 3-month monitoring schedule of BM evaluation using the currently available tools had low sensitivity to predict relapse. Findings that may justify intervention were rare (less than 10% of patients), and were restricted to abnormal cytogenetic and abnormal RT-PCR results. The clinical significance of cytogenetic abnormalities observed in donor cells is not clear. Our findings emphasize that until the optimal surveillance technique and schedule can be defined and standardized, more frequent use of pre-emptive therapy in patients at high risk of relapse may be of benefit.

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Impact of Dose Intensification of FluBu2 to FluBu4 on Transplant Related Mortality, Relapse, and Survival After Allogeneic Hematopoietic Stem Cell Transplantation for Acute Myeloid Leukemia in Remission

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Reduced intensity conditioning (RIC) with fludarabine (Flu) and sub-myeloablative doses of busulfan (Bu) (<8 mg/kg) has low transplant related mortality (TRM) compared to myeloablative (MA) conditioning, and is increasingly utilized in older and medically infirm pts. Flu with MA Bu (>5mg/kg) using pharmacokinetic (PK) dosing also has low TRM, but randomized comparisons to RIC are lacking. Therefore, we compared RIC and MA FluBu dosing on TRM, relapse and survival in remission AML. We reviewed AML pts receiving allogeneic hematopoietic stem cell transplant (HSCT) in remission (CR1/CR2) at the University of Michigan from 2003 – 2011. RIC (FluBu2) was flu 40mg/m2 x 4 days with IV Bu 3.2 mg/kg x 2 days. FluBu2 included TLI/TBI (200cGy) in 39% of cases, and ATG in one case. MA (FluBu4) was flu 40mg/m2 x 4 days with IV Bu 3.2 mg/kg x 4 days with PK adjustment to a target Css of 600-900 mcg/L (Seattle PK lab). FluBu4 had no TBI/TLI/ATG. Pt <18 yrs, cords, prior HSCT and active AML were excluded. Cumulative incidence of GVHD, TRM and relapse were calculated with competing risks. A total of 122 pts (FluBu2=71; FluBu4=51) were identified. Most primary GVHD prophylaxis was tacrol + MMF for FluBu2 (89%), and tacrol + MTX for FluBu4 (86%). FluBu2 pts were older (60 vs. 51; P < 0.1), but donor type, HLA match, and disease risk (cytogenetics / FLT3 ITD) were not significantly different. There was a trend towards higher (≥ 3) comorbidity index scores in FluBu2 (42% vs. 25%; P = 0.09). FluBu4 pts engrafted; and two graft failures occurred (3%) in FluBu2. TRM did not differ at day 100 (FluBu2=0% vs. FluBu4=2%; P = 0.3) or 1 yr (FluBu2=17% vs. FluBu4=10%; P = 0.3), but by 3 yrs there was a trend towards greater TRM in FluBu2 (FluBu2=24% vs. FluBu4=10%; P = 0.0). After adjusting for donor type, HLA match, age, and HCT-CI the trend for greater TRM in FluBu2 remained (HR: 3.5, P = 0.4, 95% CI: 1.1 – 11.0). Pts with HSTC-Cl ≥ 3, had similar TRM with FluBu2 (HR: 1.5, P = 0.6, 95% CI: 0.4 – 5.7). Acute GVHD grade II-IV was not significantly different between FluBu2 and FluBu4 (38% vs. 24%; P = 0.09). Chronic GVHD caused late deaths in 10% of FluBu2, and in 4% of FluBu4. There was no significant difference in relapse at 3 yrs (FluBu2=43% vs FluBu4=36%; P = 0.5). Overall survival (OS) favored FluBu4 compared to FluBu2 (OS: 62% vs. 39%; P = 0.02). This difference in OS was greater in intermediate risk AML (74% vs 50% P = 0.07), compared to high risk AML (40% vs 28%, P = 0.5). FluBu4 pts had a non-significant OS advantage after multivariate analysis including donor type, HLA match, and disease risk (HR: 1.75, P = 0.6, 95% CI: 1.0 – 3.1). In summary, MA conditioning with FluBu4 did not increase TRM compared to RIC with FluBu2. The potential survival benefit of FluBu4 in remission AML requires prospective validation.

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Association of Mannose Binding Lectin (MBL) Levels and Invasive Fungal Disease (IFD) in Hematologic Malignancy Patients Undergoing Hematopoietic Stem Cell Transplantation (HSCT) or Receiving Chemotherapy

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Background: IFD is a major cause of morbidity and mortality after intensive chemotherapy and HSCT in patients with hematologic malignancies. MBL is a member of the C-type lectin superfamily of microbe pattern recognition molecules. Several studies have suggested an association of MBL levels below 1,000 ng/ml with a variety of infectious complications in cancer therapy, but there are conflicting data. The aim of this study was to investigate the association between low MBL levels and the development of IFD in patients with hematologic malignancies undergoing chemotherapy or HSCT.

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<th>3 yr Nonadjusted Outcomes</th>
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<th>FluBu4 (N=51)</th>
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<tr>
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