long-term survival in pts with hematologic malignancies and compromised organ function (COF); however, pts with advanced disease do poorly with RIC alone (Giralt, Biol. Blood Marrow Transplant, 13:884, 2007). In an attempt to improve the anti-tumor efficacy of RIC, while maintaining a low-toxicity profile, we added TMLI to FLU/MEL. We hypothesize that Flu/Mel with 1200 cGY of TMLI delivered using Tomotherapy Hi-Art system is safe, tolerable, and may improve outcome in pts with COF and advanced hematological malignancies.

Patients and Methods: Pts, ≥50 years of age or COF with advanced disease status defned as high-risk remission and marrow blasts ≤10%, were eligible. The RIC consisted of FLU 25 mg/m^2/d x 5 days, MEL 140 mg/m^2 for one day, and TMLI delivered at 150 cGy/fraction in 8 fractions over 4 days.

Results: There were 16 evaluable pts (median age: 50.8 yr range 24.3–65.7 yr). The diagnoses were: AML (n = 10), ALL (n = 3), NHL (n = 2), multiple myeloma (n = 1),. At the time of HSCT 9 patients (56%) had advanced disease: 1st or 2nd relapse (n = 3), induction failure (n = 5) and progressive disease (n = 1). Seven pts (44%) were in complete remission. Mobilized peripheral blood stem cells from HLA-identical siblings (n = 7) or matched unrelated donor (n = 9) were used in all cases. Transplant-related toxicities by day +30 included: nausea grade 2 (n = 4) grade 3 (n = 12), emesis grade 2 (n = 6) and grade 3 (n = 4), mucositis grade 2 (n = 2) and grade 3 (n = 14) and fatigue grade 2 (n = 6) grade 3 (n = 4). Myeloid and platelet engraftment occurred at a median of 15 (range: 10–19 days) and 16 (range:10–19 days) days post transplant, respectively. Acute GvHD grade II-IV occurred in 38.5% of patients (grade II (31%) and grade III in 7.5%) and extensive chronic GVHD in 3 patients (19%). Five patients expired; 2 of relapsed disease, 1 with a secondary malignancy, and 2 of transplant related mortality. At a median of 12 month overall survival (OS) and disease-free survival (DFS) are 81% (95% CI, 51%–93%), and 59% (95% CI, 23%–82%), respectively.

Conclusion: The addition of TMLI at a dose to RIC with FLU/MEL appears to be tolerable and safe. The low rate of relapse and improved OS and DFS compared to historical data are promising. A study is ongoing to further assess efficacy in pts with hematological malignancies who are not eligible for RIC due to disease burden.

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CYCLOSPORINE, MYCOPHENOLATE MOFETIL AND METHOTREXATE AS POST GRAFTING IMMUNOSUPPRESSION AFTER NONMYELOABLATIVE ALLOGENEIC STEM CELL TRANSPLANTATIONS CONDITIONED WITH FLUDARABINE AND LOW-DOSE TOTAL BODY IRRADIATION

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Introduction: Nonmyeloablative (NM) hematopoietic cell transplantation (HCT) has extended the potential curative treatment option of allografting to patients in whom it was previously contraindicated due to advanced age or comorbidity. Graft-versus-host disease (GvHD), however, remains one of the major impediments to long term remission. Recently, our group has introduced a modified post grafting immunosuppression by adding methotrexate (MTX) onto the standard mycophenolate mofetil (MMF)/cyclosporin (CsP) for NMHCT recipients., with significant reduction in severe GvHD and non relapse mortality (NRM), thereby conferring favorable survival in patients receiving NMHCT. The current study is initiated to assess the feasibility and efficacy of similar approach in the setting of single institution with additional patient accrual.

Patients and Methods: Twenty-seven patients (median age, 47 years) with hematological diseases, who were poor candidates for a conventional myeloablative transplantation, receiving NM conditioning with fludarabine 90 mg/m^2 and total body irradiation (TBI) 200-cGy, followed by filgrastim-mobilized peripheral blood stem cell transplant from HLA identical (n = 26), or matched unrelated (n = 1) donors. Diagnosis include leukemia/MDS (n = 17), lymphoma (n = 2), ALL (n = 1), myeloma (n = 5) and CML (n = 2). All patients were given CSP, MMF and short course of MTX as post-grafting immunosuppression.

Results: The median times to neutrophil (500/mL) and platelet recovery (20,000/mL) were 20 and 13 days, respectively. Myelosuppression was moderate with neutrophil counts not declining below 500/mL in 5 (19%) patients, and with more than half of the patients not requiring any blood or platelet transfusion. Non-relapse mortality was low with no transplant related death occurring within the first 1 year. Overall, 11 (20%) patients had grade 2–4 acute GvHD, with only 5 (9%) patients experiencing grade 3–4 acute GVHD. Acute GVHD was diagnosed at median day +98 (range, days +33 to +158). Extensive chronic GVHD was observed in 2 of 24 evaluable patients (8.3%). Relapse-related death occurred in 6 (11%) patients. At median follow-up of 40 months (range, 20–57 months), the 4-year probability of overall and progression-free survival were 61% and 42%, respectively.

Conclusions: The addition of MTX onto the CSP and MMF as post grafting immunosuppresion offers the possibility of further optimization of GvHD control in patients receiving NMHCT, with encouraging survival.

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ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) FOR PATIENTS IN THE 6TH AND 7TH DECADES OF LIFE WITH AML OR MDS USING MYELOABLATIVE, REDUCED TOXICITY IV BUSULFAN/FLUDARABINE (BUFLU) CONDITIONING REGIMEN

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AML and MDS are moderately sensitive to the graft-versus leukemia effect, therefore making the preparative regimen dose intensity an important part of the treatment plan. For patients older than age 55, the optimal conditioning regimen prior to HSCT remains to be determined. Because of the high rates of morbidity and mortality associated with HSCT in the elderly, many patients older than 50–55 years are excluded from treatment with myeloablative conditioning regimens. Herein, we report promising findings using intravenous (IV) BuFlu myeloablative conditioning regimen in patients older than age 54 years with AML or MDS.

Methods: A cohort of 74 patients age 55 years with AML (n = 60) with high or intermediate risk cytogenetics or MDS (n = 14) with a high IPSS were transplanted in first complete remission (CR1) or with disease beyond CR1. The preparative regimen consisted of IV Flu 40 mg/m2 and IV Bu 130 mg/m2 given once daily over 3 hours on pre-transplant days -6 to -3. Graft-versus-host disease (GVHD) prophylaxis was accomplished with use of Tacrolimus and methotrexate.

Results: Median age was 58 years (range 55–66); 18 patients (24%) were older than 59 years. Fifty-four percent of patients were in complete remission (CR); 32% in first CR (CR1) and 22% in second CR (CR2); 46% had active disease. Donors were HLA-matched related (50%) and unrelated (50%). All patients engrafted. Forty-one percent and 7% of the patients had grades II-IV and III-IV acute GVHD, respectively. Chronic GVHD rate was 42%. Median follow-up is 22 months (range 1–82 months). Two-year overall survival (OS) was 70%, 48%, and 35% for patients transplanted in CR1, CR2, and with active disease, respectively. For patients in CR1, CR2, and with active disease at time of HSCT, actuarial 2-year event free survival (EFS) is 65%, 45%, and 30%, respectively. Thirty-two percent of the patients have relapsed (n = 24). Disease progression (n = 22), GVHD (n = 8), infection (n = 3), and organ failure (n = 3) were the primary causes of death. TRM and survival are shown in Table.

Conclusion: Our results show low TRM rates for selected patients in the 6th and 7th decades of life with high-risk AML and MDS who received BuFlu. Furthermore, long-term follow up indicates that responses with this regimen are stable in a significant proportion of patients. We conclude that age in itself should not be the primary reason to exclude patients from receiving myeloablative transplants.

Cumulative Incidence of Transplant-Related Mortality (TRM) by Pre-Transplant Disease Status

TRM	30-Days	100-Days	1-year
All patients	None	4%	21%
All CR (n=40)	None	5%	18%
CR1 (n=24)	None	4%	15%
Persistent Disease (n=34)	None	3%	27%