Patients diagnosed as ALL, AML or MDS with high-risk features need myeloablative conditioning regimen prior to SCT. Total body irradiation (TBI) contacting regimens have been commonly used, whereas thiotepa can mimic the effect of radiation. We would like to evaluate clinical outcomes and assess complications of haplo-identical SCT with post-transplant cyclophosphamide (PTCY) using TBI-based condition regimen (TBI-regimen) versus thiotepa (thio)-based conditioning regimen (Thio-regimen) in high-risk childhood hematologic malignancies.

We retrospectively reviewed medical record of patients with high-risk hematologic malignancies, aged less than 20 years old, between August 2012 and September 2018. HLA studying of all patients and their parents were done by high-resolution technique searching for A, B, C, DR and DQ subunits. Parents with greater HLA matching or those with presence of KIR B haplotype were chosen to be a donor for patients. Patients received TBI-regimen (low-dose TBI, fludarabine, busulfan and melphalan) during August 2012 to April 2017. While patients received Thio-regimen (thio, fludarabine and busulfan) during March 2015 to September 2018 due to an availability of thio in Thailand. Patients were given unmanipulated stem cell products on day 0, then received PTCY, and continued either a calcineurin inhibitor or an mTOR inhibitor with mycophenolate as a graft-versus-host-disease (GvHD) prophylaxis regimen. Survival analysis was calculated by Kaplan-Meier analysis and log-rank test was used to compare variables.

Forty-three patients (21 of male) were enrolled; 22, 19 and 2 patients were diagnosed as ALL, AML and MDS, respectively. Twenty-three patients received TBI-regimen, and 26 patients received mother derived stem cell products. Most of the donors had 5/10 or 6/10 HLA-matched. The median CD34+ cell dose was 9.24 (2.06-21.8) cells x 10^6/kg. One patient died from disseminated adenoviral infection prior to neutrophil engraftment. For 42 evaluable patients, the median time to neutrophil and platelet engraftment was 15 (12-26) days and 22 (12-100) days, respectively. At the median follow-up time of 18.5 (0.6-74.2) months, the overall survival rates of TBI-regimen and Thio-regimen were 63.68 and 61.98%, respectively (p=0.69), while the event-free survival rates of TBI-regimen and Thio-regimen were 68.82 and 66.67%, respectively (p=0.61). Viral infections, CMV, BKV and adenovirus, were the most common infectious complications and were comparable in both groups. Moreover, rates of acute and chronic GVHD in both groups were not significantly different. Relapse was the most common cause of death in both regimens while non-relapse mortality rates of both regimens were approximately 17%.

Haplo-identical SCT in high-risk pediatric hematologic malignancies using Thio-regimen had comparable clinical outcomes and complications as those using TBI-regimen.

**268**

**High-Dose Thiotepa-Cyclophosphamide (TT/Cy) Results in Superior Outcomes Compared with Total Body Irradiation-Cyclophosphamide (TBI/Cy) in Patients with Acute Myeloid Leukemia (AML), Advanced Chronic Myeloid Leukemia (CML) and High-Grade Myelodysplasia (MDS) Undergoing Allogeneic Hematopoietic Stem Cell Transplantation (HCT)**

in patients with myeloid malignancies undergoing allogeneic HCT, and compare the results with TBI/Cy.

**Methods:** We retrospectively analyzed 149 consecutive patients with AML (n=101), advanced CML (n=29), and high-grade MDS with >5% blasts (n=19) who received either TBI/Cy (TBI >13.5 Gy; Cy 120 mg/kg) or TT/Cy (TT 15 mg/kg; Cy 120 mg/kg) and allogeneic HCT from HLA-matched sibling or 9/10 HLA-matched volunteer unrelated donors (VUD) between 2007-2016 at Mayo University.

**Results:** Sixty-seven patients received TBI/Cy and 82 received TT/Cy. Baseline characteristics were not significantly different. TBI/Cy resulted in significantly higher grades 3-4 toxicity, including mucositis (64% vs. 46%, P=0.048), acute respiratory failure (22% vs. 10%, P=0.04), transaminase elevation (24% vs. 9%, P=0.01), acute renal failure (16% vs. 5%, P=0.02), and sinusoidal obstruction syndrome (16% vs. 0%, P=0.0001). Cumulative incidence of 100-day grades 2-4 acute GVHD (TBI/Cy 15.0% ± 4.4%, TT/Cy 20.7% ± 4.5%, P=0.15) and extensive stage chronic GVHD at 1-year (TBI/Cy 35.3% ± 6%, TT/Cy 43.6% ± 5.6%; P=0.27) were not significantly different. The cumulative incidence (CI) of non-relapse mortality (NRM) was higher following TBI/Cy (Fig 1A, P<0.001); at 1 year NRM was 31.5% ± 5.8% for TBI/Cy and 12.2% ± 3.6% for TT/Cy. There was no significant difference in the CI of relapse (CIR) (Fig 1B, P=0.49); the 3-year CIR was 21.2% ± 5.1% with TBI/Cy and 28.7% ± 5.6% with TT/Cy. The overall survival (OS) was significantly higher with TT/Cy compared with TBI/Cy at 1 year (79.3% ± 4.5% versus 52.2% ± 6.1%) and 3 years (57.3% ± 5.9% versus 35% ± 5.9%) (Fig 1C, P=0.001). On multivariable analysis, TT/Cy was associated with a significantly lower risk of death (HR 0.42; 95% CI 0.27-0.68, P<0.001), while 9/10 HLA-matched VUD and Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) >5 were both associated with a higher hazard of death (P=0.02 and P=0.004).

**Conclusion:** TT/Cy is an effective conditioning regimen in patients with myeloid malignancies undergoing allogeneic HCT and is associated with lower NRM compared with TBI/Cy. Future studies should assess whether addition of other agents to TT and Cy improve outcomes or simply increase toxicity.

**Long-Term Outcomes after Reduced-Intensity Conditioning Allogeneic Hematopoietic Stem Cell Transplantation for Acute Myeloid Leukemia and Myelodysplastic Syndrome**

**Kevin Charles Miller**1, **Moussab Damaj MD**2, **Mithun V. Shah MD, PhD**1, **William J. Hogan MD**1, **Mithun V. Shah MD, PhD**1, **William J. Hogan MD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1, **Mithun V. Shah MD, PhD**1

**Introduction:** Reduced-intensity conditioning (RIC) regimens have expanded allogeneic hematopoietic stem cell transplantation (allo-HSCT) to patients (pts) with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) who are unfit for myeloablative regimens. Several RIC regimens are typically used. We and others have previously shown that fludarabine-melphalan (FM) has a lower risk of relapse compared to fludarabine-busulfan (FB).

**Objectives:** Herein, we re-examine these findings with a larger cohort and longer follow-up. We also compare the composite endpoint graft-versus-host disease (GVHD)-free, relapse-free survival (GRFS), and elucidate factors that predict for relapse and NRM.

**Methods:** After IRB approval, we conducted a study of pts (age ≥18) diagnosed with AML or MDS who underwent allo-HSCT from January 1st, 2008 to March 1st 2017 at Mayo Clinic Rochester. Only pts who received FM (melphalan 140 mg/m²) or FB (busulfan 0.8 mg/kg IV for 10 doses with therapeutic AUC target of 900-1500 mcml/[l/min]) were included. Grade III-IV acute GVHD, systemic therapy-requiring chronic GVHD, relapse, or death counted as events for GRFS. Statistical analyses were performed using JMP 13 and EZR 1.36.

**Results:** We identified 184 pts who underwent RIC allo-HSCT: 135 with AML and 49 with MDS. The median age for the entire cohort was 61 (range, 18-74). FM was used in 123 pts, while 61 received FB. Baseline characteristics were comparable (Table 1a). The median follow-up was 5 years (95% CI, 4-5.6).

In line with previous findings, the cumulative incidence of relapse (CI-R) was significantly higher with FB compared to FM: 3-year CI-R was 31.7% for FB vs. 17.3% for FM (p=0.04) (Figure 1a). On the other hand, there was a nonsignificant trend towards an increased CI-NRM in the FM group; at Day +100, CI-NRM was 6.5% for FM vs. 1.6% for FB (p=0.24). Acute and chronic GVHD were comparable (Table 1b).

The median GRFS for the entire cohort was 7.3 months (95% CI, 6.1-8.4); there was no difference between the two regimens (p=0.94). Overall survival (OS) was comparable (p=0.61), as were causes of death (Figure 1b). In a multivariate Fine-Gray proportional hazard model for relapse vs. NRM, which included factors in Table 2; disease status (CR1 vs. CR2 or active disease) predicted relapse (HR 0.42; 95% CI 0.21-0.84, p=0.01). There was also a trend towards a decreased risk of relapse with FM (HR 0.54, 95% CI 0.28-1.03, p=0.06). On the other hand, age was predictive of NRM (HR 1.05 per year, 95% CI 1.01-1.09, p=0.01).

**Conclusion:** In the present follow-up study, there were no significant differences in GRFS or OS between FM and FB regimens for RIC allo-HSCT in AML/MDS, despite FB having a significantly higher risk of relapse. Likely, the OS was balanced by continuing NRM after FM conditioning, particularly in older pts. Further studies, ideally prospective, are required to elucidate the optimal RIC regimen matched to disease biology and pt fitness.

![Figure 1. (a).](image-url)