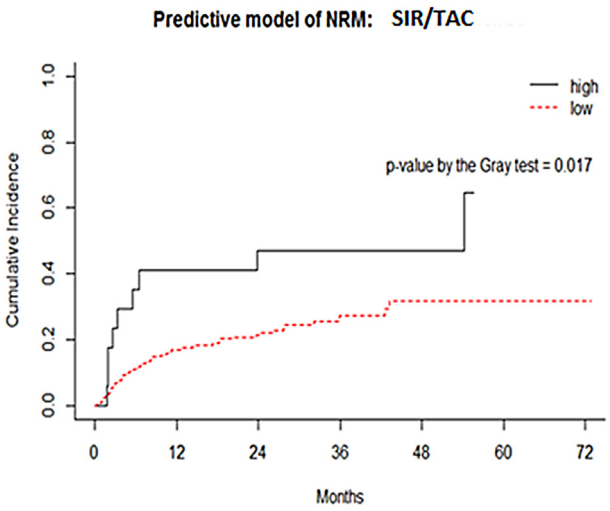
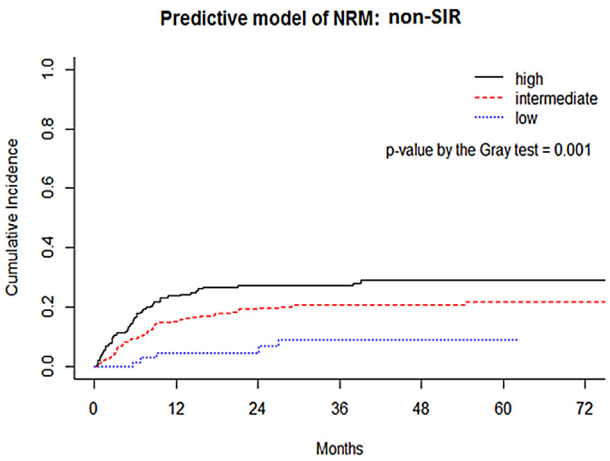


Methods: We examined a consecutive series (n=818) of allogeneic hematopoietic cell transplantation (HCT) procedures (2008-2013) performed at Moffitt Cancer Center to identify predictors of non-relapse mortality (NRM) among those that received SIR/TAC (n=308) vs. non-sirolimus based regimens; MTX/TAC (n=422) and MMF/TAC (n=88) were grouped (non-SIR) given no difference in NRM or other major HCT outcomes. Considered variables for each group included pre-HCT assessments (disease/remission status, vital organ functioning and laboratory parameters, performance status (KPS), BMI, comorbidity index (HCT-CI)), donor and recipient factors (age, gender, CMV, ABO, HLA matching, graft source, donor relation), and HCT therapy (conditioning intensity, in-vivo T cell depletion). Variables associated with NRM on univariable analysis were selected for multivariable analysis using backward elimination (final $p<0.05$ considered significant). Models were developed separately for SIR/TAC and non-SIR groups.

Results: Considered variables were well matched between groups, except donor/recipient gender, age, disease status, and donor relation ($p<0.05$). There was no significant difference in NRM, overall survival, relapse and chronic GVHD between groups, while acute GVHD was reduced among SIR/TAC patients after unrelated donor HCT (p=0.06). The incidence of TMA and SOS was higher in SIR/TAC (TMA; $P<0.001$, SOS; $P<0.001$). On multivariable analysis, unique predictors of NRM were detected for the SIR/TAC vs. other group (table 1). Predictive models based on hazard-ratio weighted scoring for these factors segregated distinct prognostic groups (figure 1).



Conclusion: These data support that routinely assessed pre-HCT variables can be used to guide selection of sirolimus- or non-sirolimus containing calcineurin inhibitor-based GVHD prophylaxis to minimize non-relapse mortality.

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The Contribution of Posttransplant RBC Transfusions and Missing Dose of Methotrexate Prophylaxis to the Development of Acute Graft Versus Host Disease in Children

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Graft versus host disease (GVHD) is an immunological complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT). Intensity of conditioning, HLA and sex mismatch, older donor age and lack of GVHD prophylaxis are the well known risk factors of GVHD development. In a recent study Giver et al showed that number of red blood cell (RBC) transfusions during the 30 days posttransplant also correlate with the severity of acute GVHD. Apart from the nearly standard regimen of prophylaxis by methotrexate and cyclosporine combination, aGVHD still occurs. We retrospectively evaluated aGVHD risk factors in our center as there are limited data on these in matched related donors in the pediatric setting.

72 transplants for 67 patients (13 girls, 54 boys, median age 8 years, range 1-16 years) were analyzed. All transplants were from matched related donors (53 matched sibling, 14 family) by myeloablative conditioning for treatment of acute lymphoblastic leukemia (ALL) (23 patients, 24 transplants), acute myeloblastic leukemia (AML) (18 patients, 19 transplants), aplastic anemia (AA) (7 severe AA patients, 3 Fanconi anemia (FA) patients, 11 transplants), thalassemia major (TM) (12 patients, 12 transplants), juvenile myelomonocytic leukemia (JMML) (3 patients, 5 transplants) and adrenoleukodystrophy (1 patient, 1 transplant). All patients except 9 (3 resistant AML, 3 FA and 3 JMML) received a standard aGVHD prophylaxis by a short course methotrexate and cyclosporine combination. Of the remaining 58 patients, 16 (27.5 %) experienced (5 patients grade I/II, 11 patients grade II/IV) aGVHD. Among the patients with grade II/IV aGVHD 3 had major ABO incompability. Posttransplant transfusion numbers in aGVHD patients (range 1-9, median 2 transfusions) were higher than the patients without aGVHD (range 1-4, median 1 transfusions) ($p > 0.05$). 6 patients (2 ALL, 4 TM) could not receive last doses of methotrexate due to severe mucositis or hepatotoxicity of whom only 2 (1 ALL, 1 TM) developed aGVHD.

This retrospective analysis showed that posttransplant RBC transfusions and missing dose of methotrexate prophylaxis do not contribute to aGVHD development in children undergoing HSCT by myeloablative conditioning.