



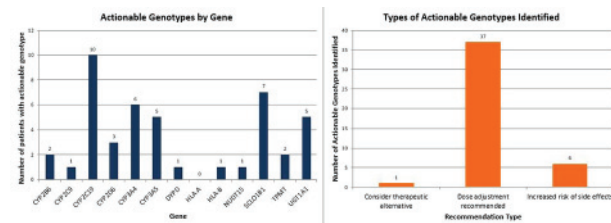
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interactions between key pharmacogenes and common supportive care medications were identified and used to guide therapy. In the absence of pediatric specific guidelines, our staff created clinical decision support, where appropriate, to standardize PGx-guided pharmacotherapy recommendations. Templates were developed to document patients' PGx results and pharmacist recommendations into the electronic health record. Frontline pharmacy staff were educated on the clinical application of PGx, workflow and goals of the service. The type and frequency of actionable gene-drug interactions, number of pharmacist recommendations for a change in drug or dose selection, and the clinician acceptance rate were analyzed. Results were compiled from admission through Day +100 post-HCT.

From February to August 2021, 33 of the 44 patients screened were eligible and PGx data were obtained. Twenty-one samples were collected in clinic and 12 results were obtained from outside hospitals. At least one clinically actionable genotype was identified in 22 patients. In total, 44 actionable genotypes were identified, 23 were relevant for HCT supportive care medications. Provider acceptance rate of pharmacy recommendations was 100%.

A process was developed that incorporates PGx data into the pharmacists' assessment of supportive care recommendations. Personalizing medication choices based on an individual's genetics helped identify the safest or most effective medication, as well as optimal dosing of supportive care medications. Implementing PGx testing in this pediatric population resulted in pharmacotherapy interventions in collaboration with providers. Future studies will examine further outcome measures and cost-benefit of the service.



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Safety and Efficacy of Prophylactic Levofloxacin in Pediatric and Adult Hematopoietic Stem Cell Transplant Patients

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Background: Levofloxacin has been widely used for bacteremia prophylaxis in the pre-engraftment setting for patients undergoing hematopoietic stem cell transplant (HSCT), but data supporting this practice are inconsistent. In addition to concern for lack of benefit, there are also concerns that this practice could increase the rates of *Clostridioides difficile* (*C. diff*) infections, the incidence of multidrug-resistant organisms (MDRO), or lead to increased incidence of acute graft versus host disease (aGVHD). This study aims to assess the safety and efficacy of levofloxacin as bacterial prophylaxis in patients undergoing HSCT at a single pediatric center.

Methods: We conducted a retrospective chart review evaluating patients six months of age and older who received an HSCT at our center between January 1, 2016, and July 31, 2020. Patients transplanted before March 2018 did not receive levofloxacin prophylaxis while patients transplanted from April 2018 did receive prophylaxis. The primary outcome of this study was the incidence of bacterial infections in the pre-engraftment phase. Secondary outcomes included: number of non-levofloxacin antibiotic days post-transplant, the incidence of aGVHD, the occurrence of *C. diff* infections, and development of MDRO.

Results: A total of 370 HSCT patients were included in this study. Seventy-two patients had more than one transplant, and therefore we had 443 transplants to observe. Of the 443 HSCTs, 216 did not include levofloxacin prophylaxis and 227 did receive prophylaxis. There were no differences in baseline characteristics between groups, except for age; patients in the non-prophylaxis group were younger (8.1 years vs. 9.6 years, $p=0.05$). Patients in the non-prophylaxis group developed more bloodstream infections in the first 100 days post HSCT (27% vs. 17%, $p=0.005$) and more *C. diff* infections than patients who received levofloxacin prophylaxis (20% vs. 9% $p = 0.003$). There was no difference in rates of death at 100 days, antibiotic use, fungal infections, or MDRO infections between the two groups. Additionally, more aGVHD was seen in the patients without prophylaxis than in the group who received levofloxacin prophylaxis ($p=0.014$).

Conclusion: Levofloxacin prophylaxis was associated with significantly decreased bloodstream infections in the first 100 days post-transplant. Additionally, levofloxacin prophylaxis was not associated with an increased risk of *C. diff*, aGVHD, or MDRO. In conclusion, our study supports levofloxacin prophylaxis use in the peri-transplant period.

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Poor Humoral Response to Sars-Cov-2 Vaccination Early after Hematopoietic Cell Transplantation: Interim Results of Prospective Study (NCT04723706)

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Background: Recent reports were published describing the immunogenicity of SARS-CoV-2 vaccine in stem cell transplant (SCT) recipients with hematological malignancies. Here we report our interim results of prospective study (NCTNCT04723706) Response to SARS-CoV-2 Vaccine in Stem Cell Transplant.

Methods and results: A total of 41 patients were recruited to be followed prospectively and longitudinally after receiving the vaccine. All patients received vaccines with doses and timing according to guidelines with some getting them as early as 3 months post SCT. We tested IgG antibodies to the SARS-CoV-2 Anti Receptor-Binding-Domain-Spike Protein. The test has a 99.1% sensitivity and 99.8% specificity for IgG antibodies to SARS-CoV-2.

33 patients had at least one IgG antibodies to the SARS-CoV-2 tested. 70% received the BNT162b2 vaccine and 30% the mRNA-1273 vaccine. Patients cohort included 16 Auto-SCT and 17 Allo-SCT. Among Auto SCT there were 3 NHL and 13 multiple

myeloma. Among Allo SCT there were 4 ALL, 8 Myeloid and 5 lymphoid with 13 MUD donors, 3 MRD and 1 MMUD. Of the 33 patients, 17 (51.5%) tested positive for SARS-CoV-2 antibodies post vaccination. The positivity rate was 50% and 53% for auto-SCT and allo-SCT recipients, respectively. In auto SCT group for patient with myeloma, rate of positivity was 61.5% however it was 0% in lymphoid malignancies with history of Rituximab exposure. In allo SCT group there was a difference between getting vaccine less than 1 year versus more than 1 year post SCT with rate of positivity 25% vs 77.7% respectively with p-value of 0.057. Also following patients prospectively and longitudinally 3 patients lost their positive humoral response including 2 allo SCT more than 1-year post SCT and one auto SCT. None of the 33 vaccinated patients were diagnosed with COVID-19 disease after vaccination.

Conclusion: In our small cohort of single center experience following SCT patients' humoral response longitudinally we found low rate of response in allo SCT especially in the first 12 months post SCT which is lower than what previously reported of 67%-37%. In addition, some patients even getting vaccine more than 1-year post SCT may lose the humoral response to the vaccine when followed longitudinally. More data is needed following 3rd booster dose and regarding cellular response to the vaccine.

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Baseline Hemoglobin Affects Outcomes after Melphalan-Based Conditioning for Allogeneic Hematopoietic Stem Cell Transplantation

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Background: Melphalan (Mel) is widely used in preparative regimens for AlloHSCT. Pharmacokinetic and clinical studies suggest wide interpatient variability in Mel exposure and toxicity using BSA-derived dosing. Mel binds to RBC membrane proteins; higher plasma Mel concentrations are seen in patients (pts) with anemia due to higher concentrations of unbound Mel. Several studies show anemia may influence outcomes after Mel in various transplant settings but it remains unclear whether this is related to diagnosis, disease risk, or other patient characteristics. We sought to study the effect of pretransplant hemoglobin on outcomes in a large uniformly treated population.

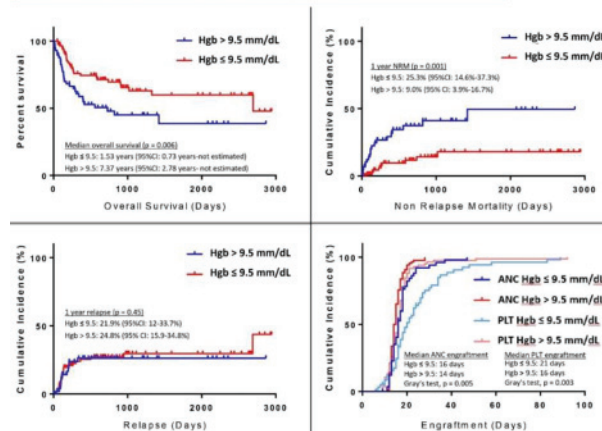
Methods: Pts who received a Flu/Mel 140 mg/m² AlloHSCT between 2012 and 2020 at a single institution were included. Pts were separated based on hemoglobin \leq 9.5 mg/dL (LowHgb) or $>$ 9.5 mg/dL (HighHgb) on the date of Mel administration. The primary endpoint was overall survival (OS). Secondary outcomes included non-relapse mortality (NRM) at 1 year (yr), incidence of relapse at 1 yr, neutrophil (ANC) and platelet (plt) engraftment, and causes of NRM between groups.

Results: Ultimately, 143 patients were included. LowHgb pts were more likely to have a diagnosis of MDS, but there was no significant differences in demographics, donor type/source, CMV status, KPS, DRI or HCT-CI \geq 3 between groups. Median OS was inferior in the LowHgb group, 1.53 yrs (95% CI 0.73 yrs-NR) vs. 7.37 yrs (95% CI 2.78 yrs-NR), $p=0.006$. NRM at 1 yr was higher in the LowHgb group vs HighHgb group, 25.3% (95% CI

14.6%-37.3%) vs 9.0% (95% CI 3.9%-16.7%), $p=0.001$. 1yr Incidence of relapse was not statistically different, 21.9% (95% CI 12.0%-33.7%) vs 24.8% (95% CI 15.9%-34.8%), $p=0.45$. Time to ANC and plt engraftment was faster in the HighHgb group, 14 days vs 16 days ($p=0.005$), and 16 vs 21 days ($p=0.003$), respectively. Of those who expired, pts with LowHgb were more likely to die from GVHD or infection 13/30 (43%) vs 5/24 (21%) in the HighHgb group, $p=0.047$. A multivariate cox model for OS, which included all baseline characteristics, revealed HighHgb and an HCT-CI of 2 (compared to 1) as the only factors significantly correlated with OS, at a HR of 0.52 (95% CI 0.30-0.87, $p=0.01$) and HR 2.68 (95% CI 1.29-5.58, $p=0.008$) respectively.

	All subjects (N=143)	Hemoglobin \leq 9.5 (N=57)	Hemoglobin $>$ 9.5 (N=86)	p-value
Age	61 (20-72)	61 (34-72)	61 (20-71)	0.47
Male	83 (58%)	28 (49%)	55 (64%)	0.09
Indication for Transplant				
AML	54 (38%)	17 (30%)	37 (43%)	0.11
MDS	32 (22%)	18 (32%)	14 (16%)	0.04
MPN	9 (6%)	6 (10%)	3 (4%)	0.16
Lymphoma	21 (15%)	6 (10%)	15 (17%)	0.34
Other	27 (19%)	10 (18%)	17(20%)	0.83
Donor type				
MRD	51 (36%)	20 (35%)	31 (36%)	0.51
MUD	71 (50%)	28 (49%)	43 (50%)	
Haplo	11 (8%)	3 (5%)	8 (9%)	
Cord	10 (7.0%)	6 (11%)	4 (5%)	
Recipient CMV +	73 (51%)	29 (51%)	44 (51%)	1.00
Donor CMV +	50 (35%)	18 (32%)	32 (37%)	0.59
PBSC	136 (95%)	55 (97%)	81 (94%)	0.70
KPS				
< 70	14 (11%)	8 (15%)	6 (8%)	0.25
\geq 70	119 (89%)	47 (85%)	72 (92%)	
HCT-CI				
0-2	89 (62%)	34 (60%)	55 (64%)	0.72
\geq 3	54 (38%)	23 (40%)	31 (36%)	
DRI				
Low	18 (13%)	5 (9%)	13 (15%)	0.41
Intermediate	91 (64%)	40 (70%)	51 (59%)	
High	34 (24%)	12 (21%)	22 (26%)	

*Data missing on 10 patients; other includes: ALL (n=6), biphenotypic leukemia (n=2), CMML (n=4), CLL (n=2), CNL (n=1), MM (n=6), non-malignant conditions (n=6), ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CLL, chronic lymphocytic leukemia; CMML, chronic myelomonocytic leukemia; CMV, cytomegalovirus; CNL, chronic neutrophilic leukemia; DRI, disease risk index; Haplo, haploidentical; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; KPS, Karnofsky performance status; MDS, myelodysplastic syndrome; MM, multiple myeloma; MPN, myeloproliferative disorder; MRD, matched related donor; MUD, matched unrelated donor; PBSC, peripheral blood stem cell.



Conclusions: LowHgb on day of Mel administration was associated with inferior OS, higher NRM, slower ANC and plt engraftment, but no difference in relapse at 1 yr. Death from infection and GVHD were more likely to occur in the LowHgb group. HighHgb remained the most significant determinant in OS on multivariate accounting for patient diagnosis, remission status, and disease risk index. This supports the existing literature that Mel exposure and transplant outcomes may be influenced by pre-transplant anemia. Future studies are needed to measure Mel concentrations to confirm these results and determine if standardized Mel exposure influences outcomes.