authentication is LDAP-based and uses components of the Zend framework. TIPS database meets the HIPAA Security Rule requirements, Title 45 CFR Part 160 and subparts A and C of Part 164.

Results: TIPS web-based workflow tool allows all medical providers involved in a patient's transplant broader accessibility to the electronic transplant data during the transplant process. Medical providers can efficiently enter and retrieve information in real-time. Center administrators are able to obtain an overview of their Program's performance, by generating real-time reports, dashboard views of patient volumes and distributions, which contribute towards programmatic quality improvement.

Discussion: TIPS has enabled us to efficiently manage patients throughout the transplant process and improve the delivery of care and data reporting. Future TIPS enhancements include direct importation of patient demographic data from Enterprise Electronic Medical Record (EMR), and connectivity to FormsNet, via AGNIS, for direct transfer of center transplant data to CIBMTR.

PHARMACY

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Population Pharmacokinetic Modeling of Thymoglobulin in Children Receiving Allogeneic-Hematopoietic Cell Transplantation (HCT): Towards Individualized Dosing to Improve Survival

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Table 1
Patient characteristics, shown as median (range) unless specified otherwise. CB: cordblood

Number of HCTs (n)	196
Number of patients (n)	183
Age (years)	6.55 (0.1-22.7)
Weight (kg)	21 (3.66-96)
BSA (m2)	0.84 (0.14-2.1)
Starting day ATG (days before transplantation)	5.1 (1-19)
Number of samples per patients (n)	12 (4-36)
Diagnosis (%)	
Malignancy	48
Immune deficiency	22
Bone marrow failure	8
Metabolic disease	13
Benign hematology	8
Stem cell source (%)	
Bone marrow	42
Peripheral blood stem cells	11
CB	43
CB plus haplo or 2nd CB	4
Transplant number (1st,2nd,3rd) (n)	183, 12, 1

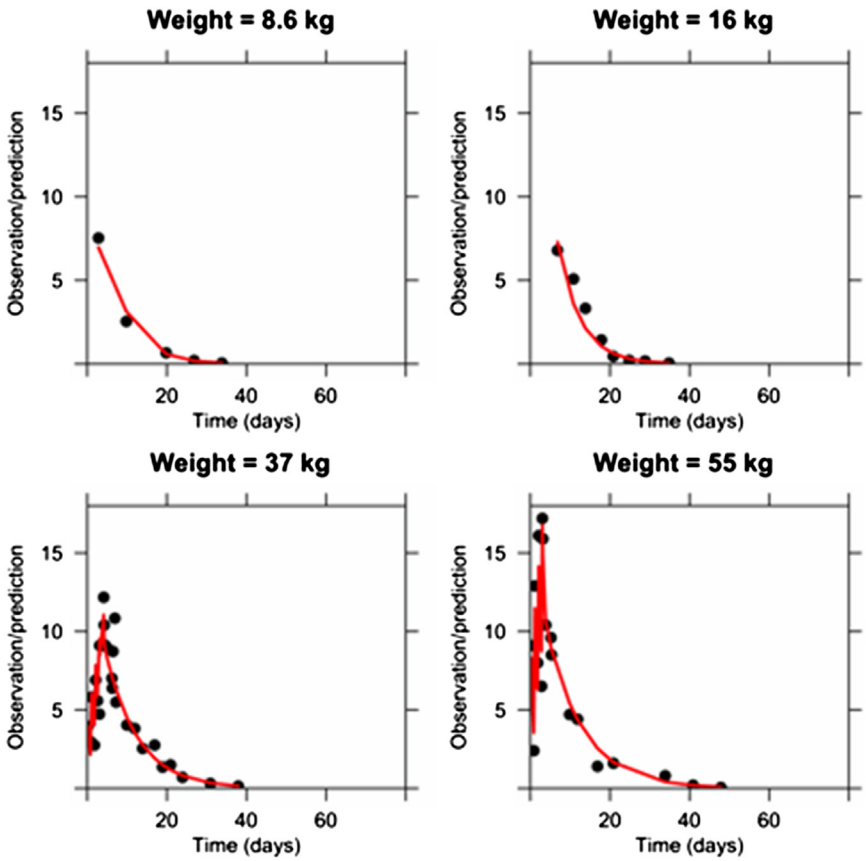

Fig 1. Observed concentrations (black dots) and individual predictions (red lines) of active Thymoglobulin versus time for representative individuals in different body weight groups.

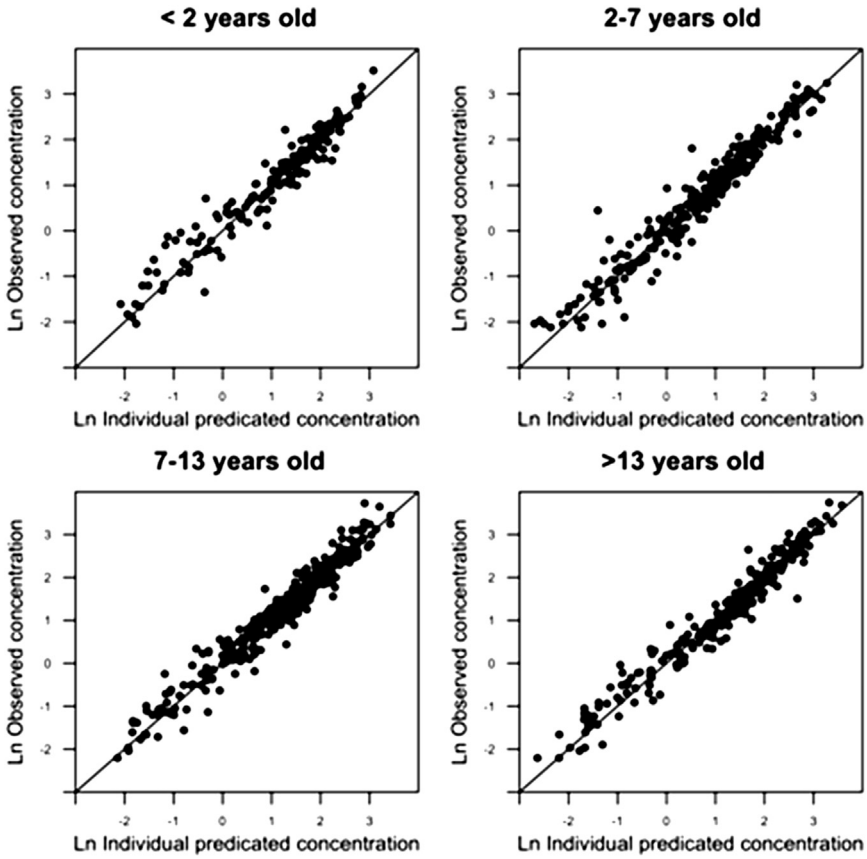

Figure 2. Observed versus individual predicted concentrations of active Thymoglobulin in all patients split by age. Dots: logtransformed observations, lines: line of unity (x=y).

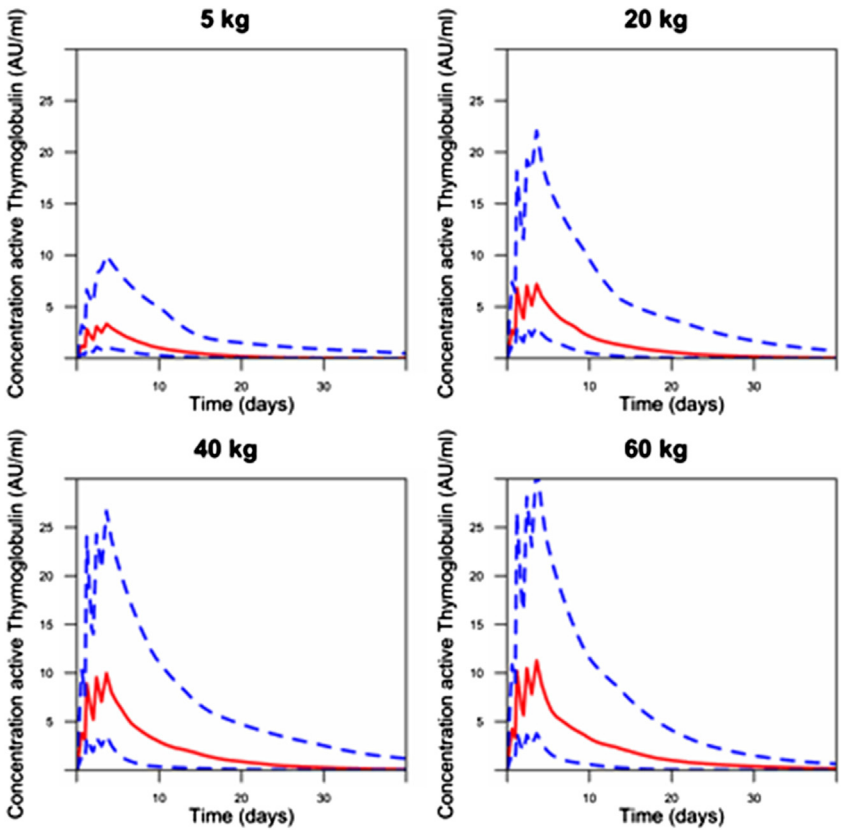

Figure 3. Median (red line) and 95% confidence interval (blue lines) active Thymoglobulin concentrations versus time in patients with a bodyweight of 5, 20, 40 and 60 kg after a cumulative dose of 10 mg/kg given over four days.

Introduction: To prevent graft versus host disease (GvHD) and rejection in hematopoietic cell transplantation (HCT), children receive anti-thymocyte globulin (ATG), a polyclonal antibody depleting T-cells, as part of the conditioning regimen. The therapeutic window is critical as over-exposure may result in delayed reconstitution of donor T-cells and increased risk of viral infections. Our objective is to describe the population pharmacokinetics (PK) of Thymoglobulin as a first step towards an evidence based dosing regimen of Thymoglobulin for HCT in children.

Methods: PK data were collected for all pediatric HCT's performed between 2004-2012 in two study centers in the Netherlands. Serum active Thymoglobulin concentrations were quantified by flow cytometry investigating the binding to a T-cell line. Population modeling and covariate analysis was performed on active Thymoglobulin concentrations using NONMEM 7.2. The final model was internally validated using advanced methods such as bootstrap resampling and NPDE.

Results: A total of 196 HCT's in 183 patients were analyzed (table 1). A two-compartment model yielded a good description of the data in all age groups (figure 1 and 2), with no evidence for non-linear elimination. The population value (SE) for clearance (Cl) and volume of distribution (Vd) of a median individual of 21 kg was 3.4 (0.2) L/day and 8.4 (0.6) L, respectively, with body weight as a significant covariate. The relationship between bodyweight and both Cl and Vd was best described by a power function with an exponent of 0.47 (0.08) and 0.62 (0.07), respectively. Terminal half-life was 4.9 days^{-1}. Figure 3 illustrates that the currently used dosing regimen of 10 mg/kg leads to higher exposure in older children compared to younger children.

Conclusion: In the validated population PK model for active Thymoglobulin in children, clearance and volume of distribution proved dependent on body weight in a nonlinear manner. Therefore, children with a higher weight are exposed to higher concentrations compared to lower weight children if the currently used dosing regimen of 10 mg/kg bodyweight is used. Once the optimal therapeutic window is determined in pharmacodynamic studies, individualized (weight based) dosing guidelines of Thymoglobulin can be derived leading to better outcome after pediatric HCT.

Table 1
AML- Acute myeloid leukemia; HLH - Hemophagocytic lymphohistiocytosis; ALL- Acute lymphocytic leukemia; CR – Complete remission; N/A – Not applicable.

Patient Characteristics	
	(Numbers)
Diagnosis	
AML	8
HLH	1
MDS	3
ALL	2
Disease Status	
CR	11
N/A	3
Regimen	9
IV BU/ IV Flu IV BU/ IV Flu + Thymoglobulin (1.5 mg/kg (T-3 to T-1)	5
Regimen Intensity	
AUC 6000	8
AUC 4500	1
AUC 4000	5
Donors	
Related	5
Unrelated	9
HLA Match	
9/10	2
10/10	12
	Median (Range)
CD34 Cells Infused (cells/kg)	7 (2.7-15)
Age at the time of transplant (years)	48.5 (23-61)
Body Surface Area (m^2)	1.825 (1.5 – 2.1)
AUC Achieved prior to PK adjustment (micromole/min)	
6000	4482.5 (3652 - 5771)
4000	3221 (2556 - 4579)
Overall AUC Achieved (micromole/min)	
6000	5380.5 (4821 - 5978)
4000	4004 (3732 - 4155)
Dose Adjustment	
6000	339 (252 - 460)
4000	240 (150 - 273)
Time to Achieve Engraftment (days)	
ANC > 500 k/uL	15 (11-20)

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Intravenous(IV) Busulfan (BU) Pharmacokinetics Using Busulfan and Fludarabine (Flu) Conditioning in Institutions Where the Capability of Doing Pharmacokinetics Is Not Present

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Background: IV BU overcomes the wide variation in achieving steady state drug concentration associated with its oral administration. Many institutions are limited in using IV BU because of an inability to perform PK analysis at an institutional level. At Markey Cancer Center we utilized a unique strategy for administering IV BU in order to facilitate PK analysis at an off-site laboratory.

Methods: This is a retrospective, chart review of 14 patients admitted for allogeneic stem cell transplant between November 2012 - September 2013 who received a conditioning regimen of IV BU and IV flu. Flu (30 mg/m2) was administered daily on days T-7 through T-3. BU dosing (desired area under the curve (AUC)) was determined based on patient age and performance status based per physician discretion. BU PK calculations were performed by the Seattle Cancer Care Alliance Pharmacokinetics Laboratory, Seattle, WA. Growth factors were not used. Patients received a once-daily BU dose (based on BSA) on days T-7 and T-5. On day T-7, BU levels were collected at the end of the infusion, 15 minutes after completion of the infusion, and at 4, 5 ,6, and 8 hours after the start of infusion. Patients did not receive BU on day T-6 in order to facilitate the ability to use PK analysis to adjust the last two BU doses on T-4 and T-3.

Results: Patient characteristics are described in Table 1. The median BU AUC achieved for the myeloabalative group was 5380.5 (4821 - 5978) uMol/min and reduced intensity group was 4004 (3732 - 4155) uMol/min. Acute GVHD was observed in six and chronic in two patients. Two patients also developed cytomegalovirus related disease. One patient relapsed at day 88 with 4% blasts on bone marrow biopsy. After a median follow up 176 days all patients are alive.

Conclusions: Our results demonstrate that PK-guided IV BU-based conditioning regimens could be used in institutions where the ability to perform institutional PK is not present. More patients and longer follow-up time would be required to conclusively determine the effectiveness of this approach.

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Efficacy of Late Hematopoietic Stem Cell Mobilization 35-40 Hours after Administration of Plerixafor

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