Relationship of limited sampling strategy and adverse effects of mycophenolate mofetil in pediatric kidney transplant patients **(RELATE)**

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BACKGROUND

- Mycophenolate mofetil (MMF) is an immunosuppressant used to prevent organ rejection in pediatric kidney transplant patients
- MMF dosing can be assessed with mycophenolic acid (MPA) trough concentrations or limited sampling strategies (LSS)
  - Limited pediatric data about either therapeutic drug monitoring strategy
- Trough concentrations are a practical method of assessment, but do not correlate well with area-under-the-curve (AUC)
- At our site, two LSS, David-Neto and Filler, are used to estimate MPA AUC
  - Insufficient evidence to recommend the use of one LSS for MMF at our site, thus both are used to better estimate AUC
- This study aims to characterize effectiveness and safety associated with LSS and trough concentration of MPA in pediatrics

OBJECTIVES

Primary objectives:

- Describe the relationship between AUC estimated via LSS and adverse effects of MMF in pediatric kidney transplant patients

Secondary objectives:

- Compare clinical outcomes between MMF therapeutic monitoring practices (LSS vs. trough concentrations)
- Describe the relationship between AUC estimated via LSS and rejection (renal biopsy confirmed)

METHODS

- **Design:** Retrospective chart review
- Clinical research ethics board approved
- **Population:** Kidney transplant patients who received MMF at BC Children's Hospital (BCCH) and had at least one MPA plasma concentration from September 2013 to October 2016
- **Inclusion:** 2-20 years old inclusive who had at least 1 interpretable MPA plasma concentration drawn at steady state
- **Exclusion:** Receiving mycophenolate sodium
- **Statistics:** Descriptive statistics
- Naranjo scores were used to determine likelihood of adverse effect being associated with MMF

TABLE 1: Baseline Characteristics

	N=33
Age (mean) at time of TDM (± SD)	14. 7 ± 4.5 years
Male, N (%)	19 (58)
Type of Therapeutic Drug Monitoring, N (%)	
Limited sampling strategy sets	12 (12)
Trough concentrations	91 (88)
Mean MMF dose/BSA (± SD)	448.6 ± 118.9 mg/m^2

ADVERSE EFFECTS (AE)

Figure 1: MPA LSS

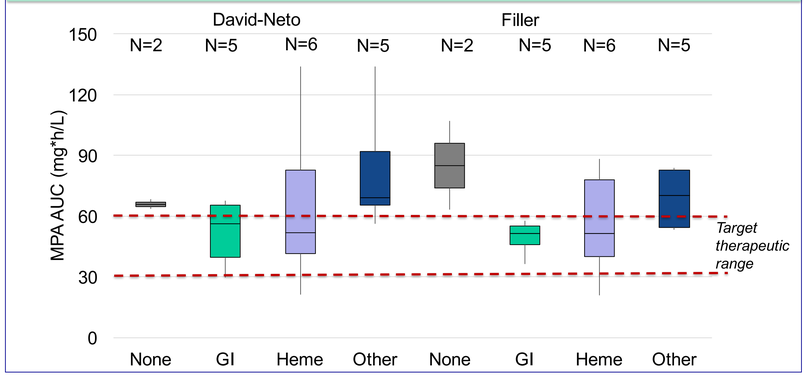


Figure 2: MPA trough concentrations

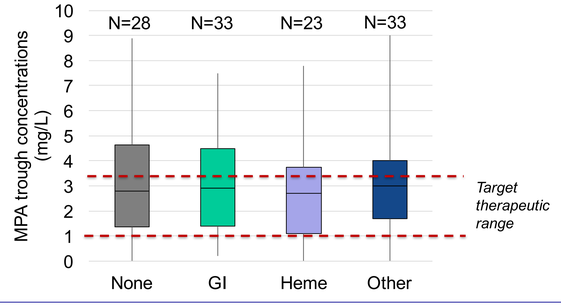
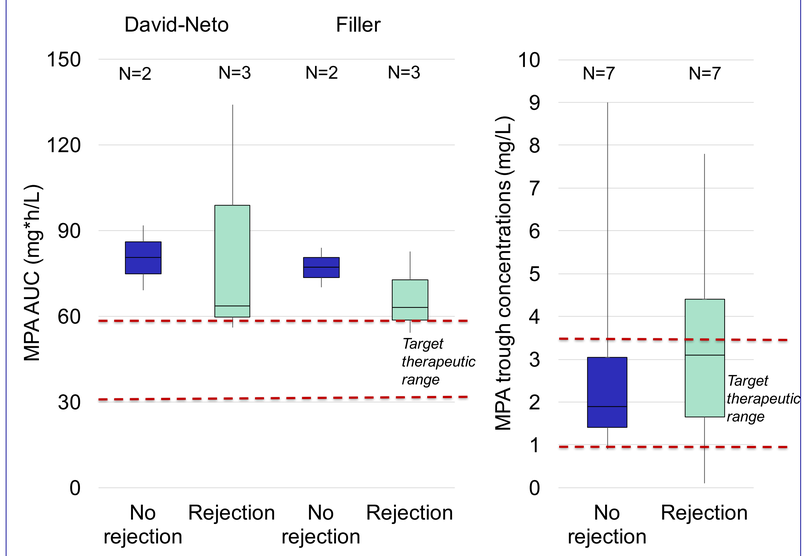


Figure 3: AE composition

EFFECTIVENESS: Rejection

Figure 4: MPA LSS and Trough Concentrations



LIMITATIONS

- Therapeutic drug monitoring may have been done more frequently in context of clinical suspicion of AE or rejection which may confound the results
- Confounders may exist which were not accounted for
- The sample size was smaller than anticipated and thus we were unable to perform the multivariate analysis that was planned

CONCLUSION

- MPA AUC estimated by limited sampling strategy, and trough concentrations of MPA did not appear to be associated with occurrence of AEs or rejection
- In light of these data, the utility of measuring MPA trough concentrations and LSS should be reassessed