CHAPTER VI

CONCLUSION

1. Our results suggested that there were relationship between gastrointestinal adverse event (GAE) and C trough (C0), C peak (C0.25, C0.5 or C1), C trough (C12) and 12-hours MPA AUC. Mean ± SE and statistically significant of these values were concluded in the table below:-

Data	Serious GAE			Mild and serious GAE		
	Mean ± SE	p - value	95%CI	Mean ± SE	P - value	95%CI
1. C0 (mcg/mL)	6.30 ± 0.57 6.49 ± 0.75	0.001 0.001	5.27-7.42 5.02-7.97	4.26 ± 0.98 4.67 ± 0.74	0.037 0.036	2.33-6.18 3.22 – 6.13
2. C0.25 (mcg/mL)	30.77 ± 10.82 35.39 ± 9.57	0.055 0.004	9.56-51.98 16.64 – 54.14	30.77 ± 10.82 19.47 ± 6.98	0.055 0.529	9.56-51.98 5.79 – 33.15
3. C0.5 (mcg/mL)	46.40 ± 0.07 51.90 ± 11.81	<0.001 0.119	46.26 - 46.54 28.75 – 75.05	45.94 ± 0.46 34.79 ± 8.84	<0.001 0.843	45.04 - 46.84 17.46 – 52.13
4. C1 (mcg/mL)	41.14 ± 0.71 46.02 ± 2.83	0.103 0.005	39.75-42.53 40.47 – 51.56	30.10 ± 7.08 36.17 ± 5.45	0.608 0.070	16.22-43.98 25.48 – 46.86
5. C12 (mcg/mL)	6.34 ± 1.71 6.70 ± 1.20	0.006 0.001	2.98-9.70 4.34 – 9.05	6.34 ± 1.71 5.13 ± 1.08	0.006 0.006	2.98-9.70 3.02 – 7.20
6. MPA AUC mcg*hr/mL)	103.92 ± 1.03 113.26 ± 7.36	0.099 0.002	101.92-105.94 98.83 – 127.70	91.76 ± 13.85 98.35 ± 9.81	0.119 0.005	64.60-118.92 79.12 – 117.59

Abbreviations; xx.xx = actual collected data
xx.xx = actual collected plus predicted data

From the result in the above table, C trough (C0) was judged as the best MPA plasma level for prediction of the occurrence of GAE since beside this plasma level was statistically significant related to GAE, C0 was the optimum sampling time in clinical practice. Based on our suggestion, C0 which was higher than 5 mcg/mL would result in high chance for the patient to experience serious GAE while C0 which higher than 3 mcg/mL could cause high chance of mild GAE. The 12-hours MPA AUC value which was higher than 79 mcg*hr/mL could possible resulted in higher risk for GAE in renal transplanted Thai patients. This value was higher than the reference range for prevention of acute renal rejection reported in Western (12-hr MPA AUC was 30 to 60 mcg*hr/mL).

2. Previous studies reported that MPA AUC could be used to predict efficacy of MMF. Our study suggested minimum blood sampling strategy of MMF that would explain both efficacy and GAE toxicity. We found the best correlated between MPA AUC and the MPA plasma level at half- hours (C 0.5; the one C peak in this study) after MMF dosing (R^2 = 0.467 and APE = 27.171 $\pm$ 5.684 %). Similarly with the study by Mourad et al.(2001) which C0.5 was correlated by R^2 = 0.599. However, the one selected time point might not provide high enough correlation between plasma level and AUC, whereas 3 (3-STP) or 4 (4-STP) selected time point models which including C0 (C0, C0.5 and C1 hours after MMF dosing or C0, C0.5, C1 and C2 hours after MMF dosing, respectively) were the optimum sampling strategy for MMF monitoring (R^2 = 0.866 and APE = 12.060 $\pm$ 2.189 % for 3-STP and R^2 = 0.940 and APE = 9.308 $\pm$ 1.495 % for 4-STP).

3. We suggest the optimum MMF dose in Thai renal transplanted patients with normal body weight and serum creatinine to be MMF 1000 mg per day which was approximately half of those doses required by Western patients.

Due to the shortage of time and the small number of patients included in this study, further studies are required for a stronger conclusion to be made.