

# TDM of MMF in >1,000 paediatric renal transplant patients using an online expert system

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## Introduction

ISBA is an online expert system routinely used since 2005 for estimating the area under the curve (AUC) of immunosuppressive drugs through pharmacokinetic modelling and Bayesian estimation, and proposing dose adjustments to reach predefined exposure targets.

**Objectives:** to describe mycophenolate-mofetil (MMF) exposure and evaluate the efficiency of ISBA dose recommendations in pediatric kidney allograft recipients.

## Methods

Database of our ISBA website (2005-2019), at <https://pharmaco.chu-limoges.fr>  
Retrospective analysis of 4051 requests in 1051 patients (mean age 13.1 y) posted by 51 kidney transplantation centers worldwide.

In 74% of the requests patients were on tacrolimus and in 18.5% on cyclosporine. 61% of the patients had >1 requests.

## Results

- In 74% of the requests patients were on tacrolimus and in 18.5% on cyclosporine.
- 61% of the patients had >1 requests.

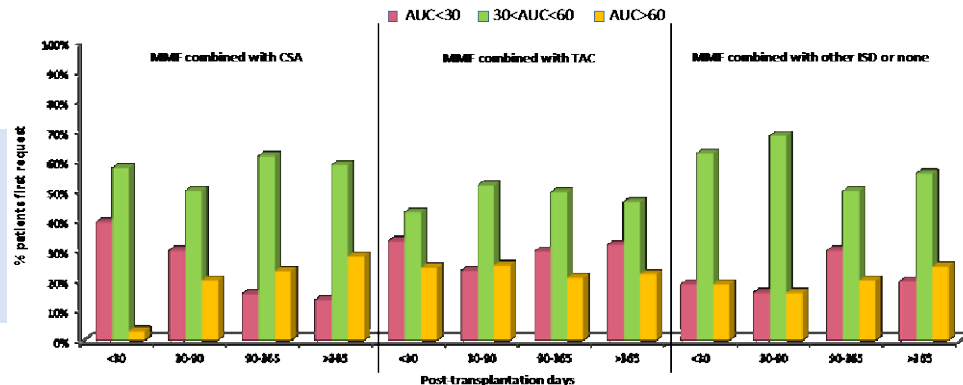


Figure 1: Distribution of MPA AUCs at the first request → only 50% in the target range

Figure 2: Distribution of MPA AUCs in patients with >1 request & same drug combination (n=472) (median and 95% intervals)

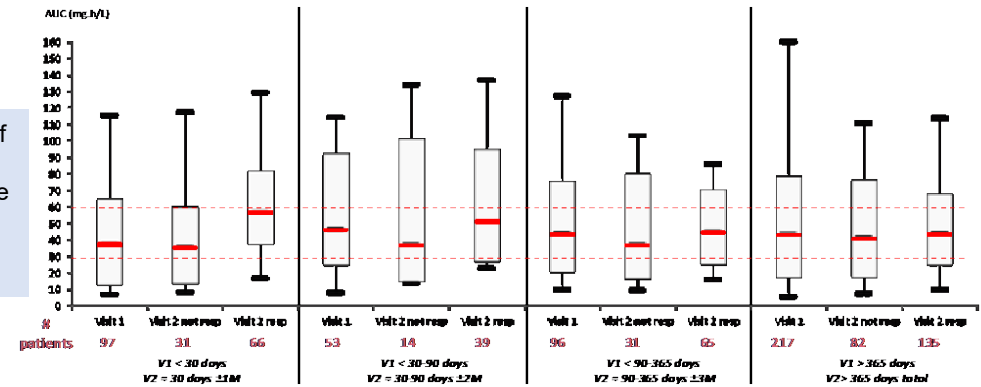


Table 1: Efficiency of dose adjustment recommendations (patients with >1 request, n=472)

	FIRST VISIT								
	MMF + CSA			MMF + TAC			MMF + another ISD or none		
	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60
< 5 years	20	871 ± 353	50%	31	487 ± 210	42%	2	460 ± 198	0%
5-10 years	25	864 ± 274	44%	83	804 ± 366	45%	5	640 ± 267	60%
10-15 years	35	1415 ± 572	74%	121	1022 ± 446	47%	5	1120 ± 926	40%
15-18 years	28	1566 ± 481	57%	109	1474 ± 473	45%	8	1588 ± 845	25%
All ages	108	1226 ± 546	58%	344	1064 ± 526	45%	20	1121 ± 784	35%
	SECOND VISIT, DOSE RESPECTED								
	MMF + CSA			MMF + TAC			MMF + another ISD or none		
	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60
< 5 years	12	887 ± 402	83%	19	615 ± 331	63%	1	800 ± 0	100%
5-10 years	17	1001 ± 460	41%	51	773 ± 315	69%	4	670 ± 363	50%
10-15 years	29	1521 ± 576	52%	75	1042 ± 347	49%	3	750 ± 177	33%
15-18 years	20	1525 ± 510	65%	78	1429 ± 515	64%	5	1500 ± 612	60%
All ages	78	1311 ± 574	58%	223	1080 ± 496	60%	13	1018 ± 572	54%
	SECOND VISIT, DOSE NOT RESPECTED								
	MMF + CSA			MMF + TAC			MMF + another ISD or none		
	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60	N patients	Mean daily dose of MMF ± SD	N patients with 30<AUC<60
< 5 years	8	778 ± 404	25%	12	519 ± 209	33%	1	500 ± 0	0%
5-10 years	8	934 ± 373	38%	32	716 ± 464	41%	1	500 ± 0	100%
10-15 years	6	1333 ± 753	33%	46	952 ± 437	48%	2	1500 ± 707	50%
15-18 years	8	1906 ± 626	63%	31	1448 ± 494	52%	3	1523 ± 1361	33%
All ages	30	1231 ± 689	40%	121	974 ± 537	45%	7	1224 ± 972	43%

## Conclusions

- 41% of the first requests posted on ISBA for MMF dose adjustment in pediatric kidney transplant recipients were late (> 1 year)
- Only 50% of all patients had MPA AUC<sub>0-12h</sub> within the recommended range of 30-60 h.mg/L at their first request
- The next AUC<sub>0-12h</sub> was more often in the target range when the MMF dose recommended by ABIS was applied than not (58-60% vs. 40-45%,  $p < 0.0001$ ) and the distribution was narrower