

MYCOPHENOLATE MOFETIL VERSUS AZATHIOPRINE AS MAINTENANCE THERAPY FOR KIDNEY TRANSPLANT RECIPIENTS

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Background

- Incidence and prevalence of kidney disease are high and increasing in Brazil and in the world.
- This fact generates a growing number of patients that could be submitted to renal transplant and therefore high costs for health systems.



Objective

 To conduct a systematic review with metaanalysis to summarize the data efficacy of mycophenolate mofetil (MMF) versus azathioprine (AZA) in the maintenance therapy of renal transplant.



Search strategy

 A search was conducted in the MEDLINE, LILACS and the Cochrane Central Register of Controlled Trials and also handsearch to identify relevant randomized controlled trials (RCTs).

• Two reviewers assessed studies for eligibility and quality independently.



Selection criteria

 RCTs in which AZA was compared with MMF for the maintenance treatment of kidney transplant recipients.



Exclusion criteria

- Studies considering:
 - Patients aged 16 or younger;
 - Multiple transplants patients;
 - Reviews or pharmacoeconomics studies.



Data analysis

- In the meta-analysis of 12 months the data were synthesized (random effects model) and results expressed as risk ratio.
- For acute rejection values <1 favors MMF, with 95% confidence intervals.
- The data of others studies were described.



Findings

- Nine RCTs and 2107 kidney transplants were evaluated.
- The majority of the sample consisted of male patients, white, middle-aged and underwent their first kidney transplant.
- The median length of follow up was 12 months (range 12-60) and the studies were conducted in the period 1995-2002.



Findings

 At 12 months AR was significantly reduced in MMF-treated recipients (risk ratio 0.62, 0.48 to 0.81) and there were no differences in graft and patients survival.



Findings

 When considering AR and graft survival, the group that used MMF showed positive results (p>0.05).

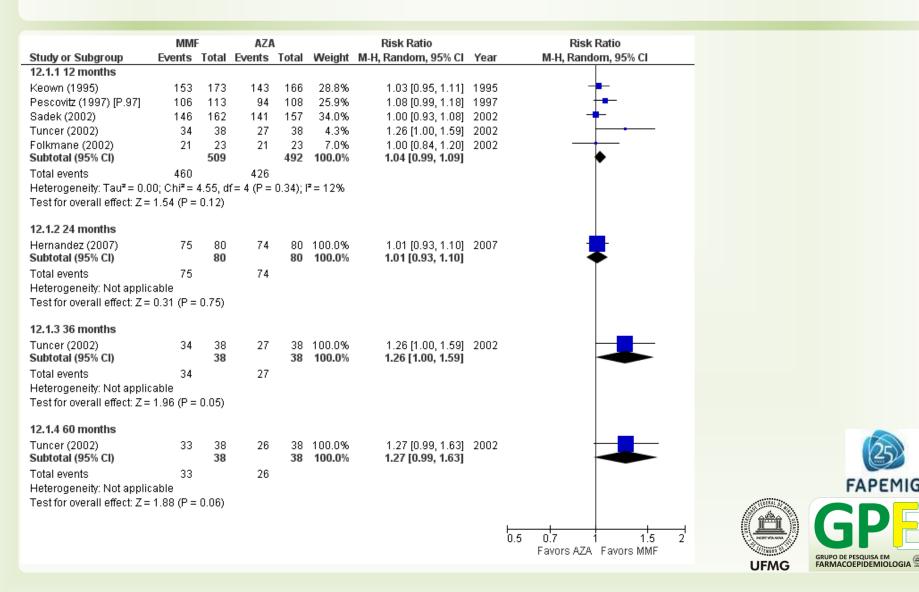
 The results of patient survival in the studies were divergent and the findings were not significant.



Acute rejection

	ММ	F	AZA			Risk Ratio		Risk Ratio
Study or Subgroup			Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
12.3.1 12 months								
Keown (1995)	37	173	60	166	57.0%	0.59 [0.42, 0.84]	1995	-
Folkmane (2002)	5	23	4	23	5.0%	1.25 [0.38, 4.07]	2002	
Sadek (2002) Subtotal (95% CI)	27	162 358	43	157 346	38.0% 100.0 %	0.61 [0.40, 0.93] 0.62 [0.48, 0.81]	2002	
Total events	69	550	107	540	100.070	0.02 [0.40, 0.01]		•
Heterogeneity: Tau ² = 0.00		43 df		י אמו∕ ו≊	- 0%			
Test for overall effect: Z = 3				1.43), 1	- 0 %			
	0.04 () = 1	0.0004,	/					
12.3.2 24 months								
Hernandez (2007)	11	80	12		100.0%	0.92 [0.43, 1.95]	2007	
Subtotal (95% CI)		80		80	100.0%	0.92 [0.43, 1.95]		•
Total events	11		12					
Heterogeneity: Not applica								
Test for overall effect: Z = I	0.23 (P =	0.82)						
12.3.3 36 months								
Pescovitz (2001) [P. 97]	44	113	71	108	100.0%	0.59 [0.45, 0.77]	2001	
Subtotal (95% CI)		113		108	100.0%	0.59 [0.45, 0.77]		•
Total events	44		71					
Heterogeneity: Not applica	able							
Test for overall effect: Z = 3	3.83 (P = I	0.0001))					
42.2.4.00 months								
12.3.4 60 months	_		4.0		400.00	0.5470.04.4.00	0000	
Tuncer (2002) Subtotal (95% CI)	7	38 38	13	38 38	100.0% 100.0 %	0.54 [0.24, 1.20] 0.54 [0.24, 1.20]	2002	
Total events	7	70	13	20	100.0%	0.54 [0.24, 1.20]		
Heterogeneity: Not applica			13					
Test for overall effect: Z = 1		0 1 2)						
restion overall ellect. Z -	1.51 (1 -	0.13)						
								0.01 0.1 1 10 100 Favors MMF Favors AZA
								FAVUIS MIMIE FAVUIS AZA

Graft Survival



Patient Survival

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Study or Subgroup	MMF Evente Total		AZA		Mojaht	Risk Ratio	Vear	Risk Ratio
Study or Subgroup 12.2.1 12 months	Events	Total	Events	Total	weight	M-H, Random, 95% Cl	rear	M-H, Random, 95% Cl
	407	470	450	400	22.60	4 04 (0 07 4 05)	4005	1
Keown (1995) Pescovitz (1997) [P.97]	167 110	173 113	159 106	166 108	23.6% 26.8%	1.01 [0.97, 1.05] 0.99 [0.95, 1.03]		I
	154	162	150	100	20.0%			1
Sadek (2002) Tuncer (2002)	104	38	37	38	8.2%	0.99 [0.95, 1.04] 1.03 [0.96, 1.10]		1
Hernandez (2007)	30 78	30 80	37 79	30 80	23.3%	0.99 [0.95, 1.03]		
Subtotal (95% CI)	70	566	79	549	100.0%	1.00 [0.98, 1.03]	2007	1
Total events	547	000	531	010	100.070	100 [0.00, 1.02]		Ĭ
Heterogeneity: Tau ² = 0.0	- · ·	116 d		0.885.1	≈ = 0%			
Test for overall effect: Z =	•			0.00/, 1	-0,0			
	0.20 () -	0.047						
12.2.2 24 months								
Hernandez (2007)	76	80	77	80	100.0%	0.99 [0.92, 1.05]	2007	-
Subtotal (95% CI)		80		80	100.0%	0.99 [0.92, 1.05]		
Total events	76		77					
Heterogeneity: Not applic	able							
Test for overall effect: Z =	0.39 (P =	0.70)						
12.2.3 36 months								
Tuncer (2002)	34	38	35	38	100.0%	0.97 [0.84, 1.12]	2002	-
Subtotal (95% CI)		38		38	100.0%	0.97 [0.84, 1.12]		-
Total events	34		35					
Heterogeneity: Not applic								
Test for overall effect: Z =	0.40 (P =	0.69)						
12.2.4 60 months								
Tuncer (2002) Subtotol (05% CI)	34	38 38	35	38 38	100.0% 100.0 %	0.97 [0.84, 1.12]	2002	
Subtotal (95% CI)	~ ~ ~	38		38	100.0%	0.97 [0.84, 1.12]		
Total events	34		35					
Heterogeneity: Not applic		0.000						
Test for overall effect: Z =	0.40 (P =	0.69)						
							L	
							0.5	
								Favors AZA Favors MMF



Conclusions

 The evidence of difference in efficacy between MMF and AZA are questionable.
Long-term hard-endpoint data from methodologically robust RCTs are still needed.



End

• Thanks for the opportunity!

