

Supplemental material

Table S1. Inclusion, exclusion and randomization criteria of Tacrolimus monotherapy in immunologically low-risk kidney transplant recipients: a randomized-controlled trial. Netherlands Trial Register [NTR4672, www.trialregister.nl]				
transplantation	inclusion	aged ≥ 18 years peakPRA $< 5\%$ HLA mismatch < 4 absence of immunological renal disease	exclusion	ABO-incompatibility CDC or FACS positive crossmatch multi-organ transplantation females of childbearing potential unwilling to use effective means of contraception
month 6	Randomization	eGFR > 30 ml/min proteinuria ≤ 50 mg/mmol in spot urine		biopsy-proven rejection after 3 months lymphocyte depleting therapy

PRA: Panel-reactive antibody CDC: Complement-dependent cytotoxicity FACS: fluorescence activated cell sorting
HLA: human leukocyte antigen eGFR: estimated glomerular filtration rate

Table S2. Tacrolimus and mycophenolate mofetil trough levels in kidney transplant recipients using tacrolimus with and without mycophenolate mofetil 6, 9, 12 and 15 months after transplantation.							
	TACmono			TAC/MMF			<i>p-value</i> (of levels outside target level)
N	34			38			
	Median in ug/L (TAC) or mg/L (MMF) (IQR)	Below range %	Above range %	Median in ug/L (TAC) or mg/L (MMF) (IQR)	Below range %	Above range %	
Tacrolimus							
M6	7.4 (2.8)	9	44	7.2 (2.8)	24	29	0.98
M9	6.3 (1.8)	15	18	5.9 (1.9)	18	5	0.29
M12	6.1 (1.8)	18	12	6.2 (1.3)	18	8	0.44
M15	6.3 (1.1)	18	6	6.1 (1.6)	16	11	0.79
Mycophenolate mofetil							
M6	2.2 (1.5)	35	15	1.8 (1.4)	29	18	0.83
M9	-	-	-	1.5 (1.4)	32	13	-
M12	-	-	-	2.0 (2.1)	29	32	-
M15	-	-	-	1.9 (2.0)	32	24	-

N: number TAC: tacrolimus MMF: mycophenolate mofetil IQR: interquartile range

M6: 6 months after transplantation M9: 9 months after transplantation M12: 12 months after transplantation

M15: 15 months after transplantation.

Table S3. Effect of Mycophenolate Mofetil dose adaptations on diarrhea in the first year after kidney transplantation.

Adaptation	n	Time	Mean diarrhea score	SE	95% Confidence Interval	
					Lower Bound	Upper Bound
Increased dose	8	M6	1.4	0.5	0.40	2.46
		M12	1.9	0.4	1.06	2.66
Unchanged dose	15	M6	1.4	0.4	0.70	2.11
		M12	1.7	0.3	1.19	2.28
Decreased dose	45	M6	2.4	0.2	1.98	2.81
		M12	1.7	0.2	1.35	1.20

M6: 6 months after kidney transplantation M12: 12 months after kidney transplantation

SE: standard error of the mean

Table S4. Upper and lower gastrointestinal symptoms in kidney transplant recipients treated with tacrolimus with mycophenolate mofetil versus tacrolimus without mycophenolate mofetil.

Time	Category	TACmono	TAC/MMF	<i>p-value</i>
Month 6	Upper	1.64 (0.81)	1.65 (0.86)	0.96
	Lower	1.64 (0.81)	1.65 (0.86)	0.96
Month 12	Upper	1.56 (0.75)	1.44 (0.60)	0.44
	Lower	1.68 (0.95)	1.82 (0.85)	0.50
Month 15	Upper	1.52 (0.80)	1.62 (0.71)	0.57
	Lower	1.76 (0.87)	1.97 (1.01)	0.34

*Repeated measures analysis

Mean scores and standard deviations are reported per upper and lower category.

TACmono: tacrolimus monotherapy TAC: tacrolimus MMF: mycophenolate mofetil

Table S5. The course of severe gastrointestinal symptoms in kidney transplant recipients from 6 months onwards per treatment group.

Time	Dimension	Overall mean (SD)	TAC-mono mean (SD)	TAC/MMF mean (SD)
Month 6	Abdominal pain n= 33	2.7 (0.88)	2.7 (1.01)	2.7 (0.81)
	Reflux n=12	2.8 (1.01)	2.6 (0.55)	2.9 (1.35)
	Indigestion n= 34	2.7 (1.04)	2.6 (1.01)	2.8 (1.10)
	Constipation n=23	2.8 (1.10)	2.6 (1.03)	2.9 (1.17)
	Diarrhea n=31	3.3 (1.30)	3.8 (1.52)	2.8 (0.83)
Month 12	Abdominal pain		2.0 (1.00)	1.8 (1.02)
	Reflux		1.2 (0.45)	1.9 (0.90)
	Indigestion		2.0 (0.88)	2.1 (0.95)
	Constipation		2.4 (1.12)	2.7 (1.60)
	Diarrhea		1.7 (0.96)	2.3 (1.30)
Month 15	Abdominal pain		2.1 (1.12)	1.8 (0.90)
	Reflux		1.4 (0.89)	1.7 (1.11)
	Indigestion		2.1 (1.03)	2.3 (0.83)
	Constipation		2.2 (1.17)	3.2 (1.64)
	Diarrhea		2.0 (1.13)	2.3 (1.29)
Change over time from 6 till 15 months after transplantation.				
		Δ score	Δ score	p-value[#]
	Abdominal pain	-0.6	-0.9	0.87
	Reflux	-1.2	-1.2	0.96
	Indigestion	-0.5	-0.5	0.95
	Constipation	-0.4	+0.3	0.39
	Diarrhea	-1.8	-0.5	0.03

*Repeated measures analysis

TACmono: tacrolimus monotherapy TAC: tacrolimus MMF: mycophenolate mofetil SD: standard deviation

N: number Δ: change

Table S6. Diarrhea multivariate analysis			
Time	Variabele	Correlation	<i>p-value</i>
Month 6	BMI	0.043	0.98
	Sex	0.385	0.71
	Age	0.015	0.50
	eGFR	0.011	0.66
	Proteinuria	0.022	0.77
Month 12	BMI	0.03	0.53
	Sex	0.277	0.27
	eGFR	0.007	0.14
	Proteinuria	0.010	0.22
Month 15	BMI	0.03	0.66
	Sex	0.30	0.11
	eGFR	0.008	0.69
	Proteinuria	0.009	0.47

BMI: body mass index eGFR: estimated glomerular filtration rate

Table S7. Gastrointestinal complaints in kidney transplant recipients with and without recent antibiotic use.			
	With recent antibiotic use (n=16)	Without recent antibiotic use (n=128)	<i>p-value</i>
Abdominal pain	1.6	1.6	0.62
Reflux	1.3	1.3	0.68
Indigestion	1.5	1.8	0.12
Constipation	2.1	1.8	0.44
Diarrhea	1.9	1.7	0.49

N: number

Table S8. Gastrointestinal symptoms in men versus women six months after kidney transplantation.			
Dimension	Sex	Mean	<i>p-value</i> <i>Bonferroni correction:</i> <i>significance level <0.01</i>
Abdominal pain	Male	1.56	0.04
	Female	1.87	
Indigestion	Male	1.78	0.40
	Female	1.90	
Reflux	Male	1.31	0.28
	Female	1.45	
Constipation	Male	1.66	0.03
	Female	2.03	
Diarrhea	Male	1.77	0.09
	Female	2.08	