NICE National Institute for Health and Care Excellence

Multiple Technology Appraisal

Immunosuppressive therapy for kidney transplantation in adults (review of technology appraisal guidance 85)

Committee papers

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MULTIPLE TECHNOLOGY APPRAISAL

Immunosuppressive therapy for kidney transplantation in adults (review of technology appraisal guidance 85) [ID456]

Contents:

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Did your systematic review include studies in patients starting a new immunosuppressive regimen at the time of a second or subsequent transplant?
Yes, such trials would have been included if patients were randomised at the time of transplantation.

If so, were any such studies identified, or do you know if any such patients were included in the studies we have discussed already?
Please see attached table for full details. However, there were 40 studies where patients received their first transplant, 14 studies did not report this, for the remainder of the studies the majority of the population (approx. 90%) received their first transplant.

If not, would it be possible to review whether these types of study were excluded during the screening stages of the SR, or to expand the SR to see whether any published studies are available?
Not applicable, because they would not have been excluded.

We did not include evidence about switching regimens while maintaining a functioning graft, since we only included studies which randomised at or around the time of transplantation. There may be some evidence about what proportion of “1st-line” patients switched and received “2nd-line” regimens, but there would be no estimates of the effectiveness for the 2nd-line regimens.

Study id	Induction therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Bingyi 2003[81]	BAS vs PBO	Primary cadaveric kidney transplant	6/6 (100%) vs 6/6 (100%)	NA	NA
Kahan 1999[67]		Primary renal transplant	173/173 (100%) vs 173/173 (100%)	NA	NA
Lawen 2003[69]		First or second cadaveric renal transplant, excluded those who had received any immunosuppressive investigational drugs within 6 months of study entry	53/59 (89.8%) vs 56/64 (87.5%)	6/59 (10.2%) vs 8/64 (12.5%)	NA
Nashan 1997[66]		Primary renal transplant	190/190 (100%) vs 186/186 (100%)	NA	NA
Ponticelli 2001[68]		First or second kidney transplant	NR	NR	NR
Albano 2013[87]	BAS vs no induction	Primary kidney/retransplantation (unless the graft was lost due to rejection within 12 months after first transplant	267/283 (94.3%) vs 288/302 (95.4%)	16/283 (5.7%) vs 12/302 (4%)	0/283 (0%) vs 2/302 (0.7%)
Sheashaa 2003[83]		Receiving their first transplant	50/50 (0%) vs 50/50 (0%)	NA	NA
Charpentier 2001[82]	ATG vs no induction	NR	NR	NR	NR
Samsel 2008[84]		Primary deceased donor kidney	29/29 (100%) vs 33/33 (100%)	NA	NA
Sheashaa 2008[85]		First live donor renal transplantation	40/40 (100%) vs 40/40 (100%)	NA	NA
Charpentier 2003[88]		Undergoing first kidney transplant or retransplantation from cadaveric donors	174/186 (93.5%) vs 170/185 (91.9%)	10/186 (5.4%) vs 14/185 (7.6%)	2/186 (1.1%) vs 1/185 (0.5%)

Study id	Induction therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Brennan 2006[89]	BAS vs rATG	Patients were excluded if they had been receiving immunosuppressive therapy before transplantation, had investigational medication within past 30 days	125/141 (88.6) vs 124/137 (90.5%)	Repeated transplant: 16/141 (11.3%) vs 13/137 (9.5%)	
Lebranchu 2002[90]		Undergo first cadaveric kidney transplantation	50/50 (100%) vs 50/50 (100%)	NA	NA
Mourad 2004[91]		Receiving first or second kidney transplant	49/52 (94%) vs 48/53 (90.6%)	3/52 (5.8%) vs 5/53 (9.4%)	NA
Sollinger 2001[92]		Receive a first or second live-donor or cadaveric renal transplant	64/70 (91%) vs 59/65 (91%)	6/70 (9%) vs 6/65 (9%)	NA
Kyllonen 2007[86]	BAS vs rATG vs no induction	Recipients of first or repeated deceased donor kidney transplants	52/58 (89.7) vs 50/53 (94.3%) vs 41/44 (93.2%)	6/58 (10.3%) vs 3/53 (5.7%) vs 3/44 (6.8%)	NA

Study (multiple publications)	Maintenance therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Schleibner 1995[93]	Tac + Aza vs CsA + Aza	Primary renal transplantation	31/31 (100%) vs 16/16 (100%)	NA	NA
Laskow 1996[94] (Vincenti 1996)[95]		Primary cadaveric kidney transplant (low tac vs med tac vs hig tac vs CSA)	33/33 (100%) vs 30/30 (100%) vs 29/29 (100%) vs 28/28 (100%)	NA	NA
Mayer 1997[96] (Mayer 2002, 1999)[97 98]		NR	274/303 (90.4%) vs 130/145 (89.7%)	Retransplant: 29/303 (9.6%) vs 15/145 (10.3%)	
Radermacher 1998[99]		NR	25/28 (89.3%) vs 11/13 (84.6%)	2/28 (7.1%) vs 2/13 (15.4%)	1/28 (3.6%) vs 0/13 (0%)
Jarzembowski 2005[100]		Primary cadaveric renal transplantation	14/14 (100%) vs 21/21 (100%)	NA	NA
Baboolal 2002[101]		NR	NR	NR	NR
Campos 2002[102]		NR	80/85 (94%) vs 78/81 (96%)	5/85 (6%) vs 3/81 (4%)	NA
Margreiter 2002[103] (Kramer 2005[104] & Kramer 2008[105])		NR	267/286 (93.4) vs 252/271 (93.0%)	One or two previous: 19/286 (6.6%) vs 19/271 (7.0%)	
Van Duijnhoven 2002[73]		NR	9/11 (81.8%) vs 9/12 (75%)	Retransplant: 2/11 (18.2%) vs 3/12 (25%)	
Waller 2002[74] (Murphy 2003)[106]		NR	46/52 (88%) vs 44/50 (88%)	5/52 (10%) vs 4/50 (8%)	
Charpentier 2003[88]		Undergoing first kidney transplant or retransplantation from cadaveric donors	174/186 (93.5%) vs 158/184 (85.9%)	10/186 (5.4%) vs 26/184 (14.1%)	2/186 (1.1%) vs 0/184 (0%)
Toz 2004[107]					NR

Study (multiple publications)	Maintenance therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Hardinger 2005[108] (Brennan 2005)[109]		De novo renal transplant recipients	134/134 (100%) vs 66/66 (100%)	NA	NA
Sollinger 1995[75]	CsA + MMF low vs CsA + AZA vs CsA + MMF	Primary cadaveric renal allograft as their first transplant	167/167 (100%) vs 166/166 (100%) vs 166/166 (100%)	NA	NA
Tricontinental MMF renal study 1996[110] (Mathew 1998,[111] Clayton 2012[112])		First or second cadaveric renal transplant	149/173 (86.1) vs 148/166 (89.2%) vs 146/164 (89.0%)	24/173 (13.9%) vs 18/166 (10.8%) vs 18/164 (11.0%)	NA
Sadek 2002[113]	CsA + MMF vs CsA + AZA	First cadaveric or living donor kidney transplant	162/162 (100%) vs 157/157 (100%)	NA	NA
Tuncer 2002[76]		First-graft cadaveric or living-donor renal transplant	38/38 (100%) vs 38/38 (100%)	NA	NA
Merville 2004[114]		Receiving their first ABO-compatible cadaver kidney transplant	37/37 (100%) vs 34/34 (100%)	NA	NA
Remuzzi 2007[115] (The MYSS trial, Remuzzi 2004[116])		First kidney transplant from deceased donors	124/124 (100%) vs 124/124 (100%)	NA	NA
Wlodarczyk 2005[117] (Wlodarczyk 2002[118])	TAC + MMF vs TAC + AZA	Primary renal transplant or transplantation	229/243 (94.2%) vs 234/246 (95.1%)	14/243 (5.8%) vs 12/246 (4.9%)	NA
Vacher-Coponat 2012[119]			NR		
Zadrazil 2012[120]	TAC + MMF vs CsA + MMF		NR		
Hernandez 2007[121]		Primary renal transplantation	80/80 (100%) vs 80/80 (100%)	NA	NA
Rowshani 2006[122]		Renal transplant recipients of a first or second graft	NR	NR	NR

Study (multiple publications)	Maintenance therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Yang 1999[123] (Ulsh 1999[124])		First cadaveric or living related renal transplant	30/30 (100%) vs 30/30 (100%)	NA	NA
Weimer 2006[125] (Weimer 2005[126])	TAC + AZA vs CsA + AZA vs CsA + MMF	NR	24/28 (86%) vs 22/25 (88%) vs 26/31 (84%)	4/28 (14%) vs 3/25 (12%) vs 5/31 (16%)	NA
Wlodarczyk 2009[127]	TAC + MMF vs TAC PR + MMF	NR			
Kramer 2010[53] (NCT00189839)		Not clear, but likely retransplantation permitted: exclusion criteria: previous nonrenal transplant; panel reactive antibody level >50% in the previous 6 mo and/or previous graft survival <1 year due to immunological-related graft loss			
Tsuchiya 2013[128]		NR			
Oh 2014[129]					
Albano 2013[87] (NCT00717470) OSAKA Trial	TAC + MMF vs TAC PR 0.2 + MMF vs TAC PR 0.3	Primary kidney/retransplantation (unless the graft was lost due to rejection within 12 months after first transplant	296/309 (95.8%) vs 288/302 (95.4%) vs 285/ 304 (93.8%)	13/309 (4.2%) vs 12/302 (4.0%) vs 17/304 (5.6%)	0/309 (0%) vs 2/302 (0.7%) vs 2/304 (0.7%)
Ciancio 2008[130] (Ciancio 2011[131]), R01DK25243-25)	MMF + TAC vs MPS + TAC	Primary kidney transplant from a deceased or living donor	29/29 (100%) vs 31/31 (100%)	NA	NA
Salvadori 2004[132]	MMF + CsA vs MPS + CsA	Received a first… …kidney transplant	210/210 (100%) vs 213/213 (100%)	NA	NA
Vincenti 2005[133] (Vincenti 2010[134])	BEL low+ MMF vs BEL high + MMF vs CsA + MMF	Patients who had previously undergone renal transplantation, patients with a … …could make up no more than 10% of the study population	NR	NR	NR
BENEFIT (Vincenti 2010[54], Larsen 2010[55],		Exclusion: retransplants with a panel reactive antibody >30% (also includes not available: 1% vs 1% vs 2%)	97% vs 96% vs 94%	2% vs 2% vs 4%	0% vs 1% vs 0%

Study (multiple publications)	Maintenance therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Vincenti 2012[56], Rostaing 2013[57])					
BENEFIT EXT (Durrbach 2010[135] Medina Pestana 2012[136], Charpentier 2013[137] Larsen 2010[55])		De novo adult recipients (from pestana)	175/175 (100%) vs 184/184 (100%) vs 184/184 (100%)	NA	NA
Ferguson 2011[138]	BEL+MMF vs BEL+SIR vs TAC+MMF	NR	32/33 (97%) vs 26/26 (100%) vs 30/30 (100%)	1/33 (3%) vs 0/26 (0%) vs 0/30 (0%)	NA
Lorber 2005[139]	EVL low + CsA vs EVL high + CsA vs MMF+CsA		NR		
ATLAS Vitko 2005[140] (Vitko 2004[141] & 2005b[142])		De novo renal transplant	194/194 (100%) vs 198/198 (100%) vs 196/196 (100%)	NA	NA
Takahashi 2013[143]	EVL + CSA vs MMF + CSA	Primary kidney transplant	61/61 (100%) vs 61/61	NA	NA
Chadban 2013 (SOCRATES)[144]	EVL vs EVL +CsA vs CsA + MPS	De novo kidney transplant recipients	49/49 (100%) vs 30/30 (100%) vs 47/47 (100%) vs	NA	NA
Tedesco Silva 2010[145]	EVL low + CsA vs EVL high + CsA vs MPA + CsA	Primary kidney transplant	277/277 (100%) vs 279/279 (100%) vs 277/277 (100%)	NA	NA
Bertoni 2011[146]	EVL + CsA vs MPS + CsA		NR		

Study (multiple publications)	Maintenance therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Budde 2011[147] (Budde 2012[148] , Liefeldt 2012[149], NCT00154310)	EVL + MPS vs CsA + MPS	Exclusion: retransplants	155/155 (100%) vs 145/145 (100%)	NA	NA
Mjornstedt 2012[150] (NCT00634920)		Receiving first or second kidney transplant	93/102 (91.2%) vs 94/100 (94%)	9/102 (8.8%) vs 6/100 (6%)	NA
Barsoum 2007[151]	SRL + CsA vs MMF + CsA	De novo transplants	76/76 (100%) vs 37/37 (100%)	NA	NA
Stallone 2003[152]			NR		
Anil Kumar 2005[153]	SRL + TAC vs MMF + TAC		NR		
Mendez 2005[154] (Gonwa 2003[155])			NR		
Sampaio 2008[156]			NR		
Gelens 2006[157]		Excluded: high immunological risk (panel reactive antibody grade >85% in the previous 6 mo and/or having a previous graft survival <1 year due to rejection	18/18 (100%) vs 16/18 (89%)	0/18 (0%) vs 2/18 (11%)	NA
Gallon 2006[158] (Chhabra 2012[159])		NR	37/37 (100%) vs 45/45 (100%)	NA	NA
Van Gurp 2010[160]		Primary renal transplantation or replantation (unless the graft was lost due to rejection within the previous 12 months); also includes 0/318 vs 1/316 (0.3%) for three previous transplants	306/318 (96.2%) vs 301/306 (95.3%)	12/318 (3.8%) vs 14/316 (4.4%)	0/318 vs 0/316 (0%)
Flechner 2002 (Flechner 2004, 2007)	SRL + MMF vs CsA + MMF	Excluded: prior transplantation	31/31 (100%) vs 30/30 (100%)	NA	NA
Noris 2007[161] (Ruggenenti 2007[162])		Primary kidney transplant recipients	11/11 (100%) vs 10/10 (100%)	NA	NA

Study (multiple publications)	Maintenance therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Lebranchu 2009[163] (Servais 2009[164], Lebranchu 2011[165], Joannides 2011[166], 2004-002987-62)		First renal transplant	95/95 (100%) vs 97/97 (100%)	NA	NA
Büchler 2007[167] (Lebranchu 2012[168], Joannides 2010[169])		NR	68/71 (95.8%) vs 66/74 (89.2%)	3/71 (4.2%) vs 8/74 (10.8%)	NA
Soleimani 2013[77]		Exclusion: prior transplantation	29/29 (100%) vs 59/59 (100%)	NA	NA
Durrbach 2008[170] (0468E1 – 100969)		First or second ECD allograft recipients		NR	
Kreis (2000)[171] - Identified from Campistol 2005[172]		Primary cadaveric donor kidney	40/40 (100%) vs 38/38 (100%)	NA	NA
Guba 2010[173]		De novo renal transplants	69/69 (100%) vs 71/71 (100%)	NA	NA
Martinez-Mier 2006[174]		Adult first degree living related kidney allograft recipient			
Nafar 2012[175] (IRCT138804333049N7)		Receiving primary or secondary kidney allograft		NR	
Larson 2006[176] (Stegall 2003[177])	TAC + MMF vs SRL + MMF	NR	66/84 (79%) vs 69/81 (86%)	18/84 (21.4%) vs 12/81 (14.8%)	NA
Schaefer 2006[78]		Primary transplants	39/39 (100%) vs 41/41 (100%)	NA	NA
Heilman 2011[178] (Heilman, 2012[179]; NCT00170053)		Exclusion: loss of previous transplant from rejection or recurrent primary disease			NR

Study (multiple publications)	Maintenance therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Welberry Smith 2008[79]			NR		
Silva 2013[180] (NCT01802268)	TAC + MPS vs SRL + MPS	De novo kindey transplant	107/107 (100%) vs 97/97 (100%)	NA	NA
Hamdy 2005[181] (Hamdy 2008[182], Hamdy 2010[183])	TAC + SRL vs MMF + SRL	Exclusion: subjects requiring a second renal transplantation	65/65 (100%) vs 67/67 (100%)	NA	NA
Charpentier 2003[184] (Groth 1999[185])	SRL + AZA vs CsA + AZA	Received a primary cadaveric donor kidney	41/41 (100%) vs 42/42 (100%)	NA	NA
Chen 2008[186]	TAC + SRL vs CsA + SRL	With their first renal transplant	21/21 (100%) vs 20/20 (100%)	NA	NA
Vitko 2006[80]	SRL low + TAC vs SRL high + TAC vs MMF + TAC	Primary renal transplantation or retransplantation (Also includes 1/325 (0.3%) for low SRL)	296/325 (91.1%) vs 302/325 (92.9%) vs 295/327 (90.2%)	26/325 (8.0%) vs 20/325 (6.2%) vs 29/327 (8.9%)	2/325 (0.6%) vs 3/325 (0.9%) vs 3/327 (0.9%)
Flechner 2011[187] (ORION study, NCT00266123)	SRL + TAC vs SRL + MMF vs MMF + TAC	Primary or secondary renal allograft	139/152 (91.5%) vs 128/139 (92.1%)	13/152 (8.6%) vs 11/139 (7.9%)	NA
Grinyo 2009[188], (SYMPHONY study Ekberg 2009[189], Demirbas 2009[190], Ekberg 2010[191], Frei 2010[192], Claes 2012[193])	MMF + CsA vs MMF + low CsA vs MMF + low TAC vs MMF low SRL (1 study)	Patients receiving a second renal transplant were eligible, providing that the first allograft was not lost owing to acute rejection within the first year after transplntation	NR		

Study (multiple publications)	Maintenance therapy	Inclusion criteria	No previous transplant n/N (%)	One previous transplant n/N (%)	Two previous transplant n/N (%)
Anil Kumar 2008[194] (Anil Kumar 2005[153]; CRG110600009)	TAC + MMF vs TAC + SRL vs CsA + MMF vs CsA + SRL	De novo kidney recipients	50/50 (100%) vs 50/50 (100%) vs 50/50 (100%) vs 50/50 (100%)		