

Appendix 6: Clinical outcomes [posted as supplied by author]

Table A: Neoral clinical outcomes

Study, year, organ	Definition of acute rejection	Trial (y/n)	Follow up time	Number of patients analyzed (I/G)	Neoral	Generic
Acute Rejection						
Khatami, 2013, kidney ⁶²	Clinical +/- biopsy	Y	1 year	221 (110/111)	16	16
Vitko, 2010, kidney ⁵⁷	Unclear	Y	180 days	99 (52/47)	0	0
Kim, 1998, kidney ⁴⁰	Unclear	Y	4 weeks	40 (20/20)	2	1
Stephan, 1998, kidney ⁵²	Unclear	Y (but only 40 were randomized)	1 year	52 (20/32)	6 biopsied, 9 presumed	5 biopsied, 14 presumed
Leet, 2009, heart ⁴²	Biopsy proven	Y	4 weeks	16	0	0
Toman, 2002, heart ⁵⁵	Biopsy proven	Y	12 weeks	11 (6/5)	0	0
Al Wakeel, 2008, kidney ³¹	Clinical +/- biopsy	N	6 months	75	8	2
Sayyah, 2007, kidney ⁴⁹	Unclear	N	6 months	41	0	0
Carnahan, 2003, kidney ³³	Unclear	N	Average follow up 18 weeks	41	0	0
Tsang, 2003, kidney ⁵⁶	Unclear	N	4 weeks	20	0	0
Roza, 2002, kidney ⁴⁸	Unclear	N	29 days (2 weeks on each)	50	0	0
Pamugas, 2012, kidney ⁴⁵	Biopsy proven	N	6 months	60 (30/30)	4	2
Spasovski, 2008, kidney ⁵¹	Unclear	N	6 months	31 (16/15)	4	9
Sharma, 2006, kidney ⁵⁰	Biopsy proven	N	1 year	37 (17/20)	8	6
Taber, 2005, kidney ⁵³	Biopsy proven	N	6 months	188 (100/88)	25	34
Kraeuter, 2013, heart ⁴¹	Biopsy proven	N	8 months	20	0	0
Graft loss (n)						
Khatami, 2013, kidney ⁶²		Y	1 year	221 (110/111)	1	0
Kim, 1998, kidney ⁴⁰		Y	4 weeks	40 (20/20)	0	0
Stephan, 1998, kidney ⁵²		Y	1 year	52 (20/32)	0	0
Al Wakeel, 2008, kidney ³¹		N	6 months	75	0	0
Pamugas, 2012, kidney ⁴⁵		N	6 months	60 (30/30)	0	0
Sharma, 2006, kidney ⁵⁰		N	1 year	37 (17/20)	1	0
Toman, 2002, heart ⁵⁵		Y	12 weeks	11 (6/5)	0	0
Kraeuter, 2013, heart ⁴¹		N	8 months	20	0	0
Death (n)						
Khatami, 2013, kidney ⁶²		Y	1 year	221 (110/111)	1	1
Vitko, 2010, kidney ⁵⁷		Y	180 days	99 (52/47)	1	0
Stephan, 1998, kidney ⁵²		Y	1 year	52 (20/32)	0	0
Al Wakeel, 2008, kidney ³¹		N	6 months	75	0	0
Roza, 2002, kidney ⁴⁸		N	29 days	50	0	0
Pamugas, 2012, kidney ⁴⁵		N	6 months	60 (30/30)	0	1
Sharma, 2006, kidney ⁵⁰		N	1 year	37 (17/20)	0	0
Toman, 2002, heart ⁵⁰		Y	12 weeks	11 (6/5)	0	0
Kraeuter, 2013, heart ⁴¹		N	8 months	20	0	0
Infection (n)						
Khatami, 2013, kidney ⁶²		Y	1 year	221 (110/111)	7	9
Vitko, 2010, kidney ⁵⁷		Y	180 days	99 (52/47)	7	7
Fradette, 2005, kidney ³⁷		N	35 days	37	2	1

Pamugas, 2012, kidney ⁴⁵		N	6 months	60 (30/30)	8	4
Toman, 2002, heart ³⁵		Y	12 weeks	11 (6/5)	0	1
eGFR (ml/min/1.73m²)						
Pamugas, 2012, kidney ⁴⁵		N	6 months	60 (30/30)	62.03 (12.1)	74.02 (15.8)
Kraeuter, 2013, heart ⁴¹		N	8 months	20	59.93 (21.98)	59.57 (20.23)
Serum creatinine (µmol/L)						
Khatami, 2013, kidney ⁶²		Y	1 year	221 (110/111)	117.5 (53.0)	107.8 (17.6)
Qazi, 2006, kidney ⁴⁷		Y (randomized to switch to generic vs no switch)	4 weeks post randomization	82 (9/73)	153.82 (106.08)	146.74 (43.32)
First, 1998, kidney ³⁸		Y	3 weeks	32	123.76 (35.36)	123.76 (35.36)
Kim, 1998, kidney ⁴⁰		Y	1 week	40 (20/20)	118.46 (37.13)	101.66 (15.03)
Stephan, 1998, kidney ⁵²		Y	6 months	52 (20/32)	107.85 (21.22)	106.96 (18.56)
Masri, 1996, kidney ⁶¹		Y	One year post randomization	44 (21/23)	140.56 (35.36)	129.06 (29.17)
Diarra, 2010, kidney ³⁵		N	1 month	59	165.48 (89.77)	164.48 (89.0)
Diarra, 2010, kidney ³⁵		N	3 months	59	165.48 (89.77)	167.82 (100)
Diarra, 2010, kidney ³⁵		N	6 months	59	165.48 (89.77)	176.41 (119.43)
Al Wakeel, 2008, kidney ³¹		N	6 months	75	116.1 (29.5)	119.8 (32.1)
Sayyah, 2007, kidney ⁴⁹		N	6 months pre and post conversion	41	123.76 (42.4)	118.46 (35.4)
Masri, 2005, kidney ⁴⁴		N	Pre conversion and 7 days post conversion	70	108.73	109.62
Masri, 2004, kidney ⁴³		N	21 days	Unclear	108.73	109.62
Carnahan, 2003, kidney ³³		N	2 weeks	41	151.16	148.51
Tsang, 2003, kidney ³⁶		N	2 weeks	20	120.4 (41.3)	118.5 (43.1)
Roza, 2002, kidney ⁴⁸		N	2 weeks	50	115.80 (41.55)	114.04 (38.98)
Pamugas, 2012, kidney ⁴⁵		N	6 months	60 (30/30)	108.73 (38.90)	99.01 (22.10)
Kahn, 2010, kidney, prevalent transplants ³⁹		N	1 month pre and post conversion	117	142 (6)	135 (5)
Spasovski, 2008, kidney ⁵¹		N	6 months	31 (16/15)	127.5 (43.5)	155.5 (68.6)
Sharma, 2006, kidney ⁵⁰		N	1 year	37 (17/20)	132.6 (141.44)	123.76 (53.04)
Kraeuter, 2013, heart ⁴¹		N	8 months	20	113.15 (29.17)	112.27 (32.71)

All continuous variables are reported as mean and standard deviation (SD) unless otherwise specified
I/G, I=Innovator, G=generic

Table B: Prograf clinical outcomes

Study, year, organ	Definition of acute rejection	Trial	Follow up time	Number of patients analyzed (I/G)	Prograf	Generic
Acute rejection						
Min, 2013, kidney ⁶⁸	Biopsy proven with clinical evidence	Y	6 months	93 (38/55)	2	2
Alloway, 2012, kidney ⁶³	Unclear	Y	28 days	71	0	0
Rosenborg, 2014, kidney ⁶⁹	Unclear	N	4 weeks	67	0	0
McDevitt-Potter, 2011, kidney, liver, multiorgan ⁷²	Biopsy proven	N	Unclear	70	0	0
Heavner, 2013, kidney ⁶⁶	Biopsy proven	N	6 months	78 (42/36)	1	0
Marfo, 2013, kidney ⁶⁷	Biopsy proven	N	1 year	106 (33/73)	0	1
Connor, 2012, kidney ⁶⁴	Biopsy proven	N	6 months	99 (48/51)	8	9
Spence, 2012, kidney, liver, heart ⁷⁰	Biopsy proven	N	106 days	234	0	0
Momper, 2011, kidney, liver ⁷³	Unclear	N	Average 50 days	103	0	0
Yu, 2012, liver ⁷¹	Biopsy proven	N	26 weeks	117 (60/57)	5	0
Acute cellular rejection 1R (mean episodes/ patient day)						
DhungeI, 2012, heart ⁶⁵	Biopsy proven	N	6 months	65 (44/21)	0.022 (0.01)	0.023 (0.01)
Acute cellular rejection 2R (mean episodes/ patient day)						
DhungeI, 2012, heart ⁶⁵	Biopsy proven	N	6 months	65 (44/21)	0.0002 (0.001)	0.0011 (0.0025)
Acute cellular rejection 3R (mean episodes/ patient day)						
DhungeI, 2012, heart ⁶⁵	Biopsy proven	N	6 months	65 (44/21)	0.0002 (0.001)	0
Graft loss						
Min, 2013, kidney ⁶⁸		Y	6 months	93 (38/55)	0	0
Alloway, 2012, kidney ⁶³		Y	28 days	71 (36/35)	0	0
Connor, 2012, kidney ⁶⁴			6 months	99 (48/51)	6	8
Yu, 2012, liver ⁷¹		N	6 months	117 (60/57)	0	0
Death						
Min, 2013, kidney ⁶⁸		Y	6 months	93 (38/55)	1	0
Connor, 2012, kidney ⁶⁴		N	6 months	99 (48/51)	2	2
Spence, 2012, kidney, liver, heart ⁷⁰		N	106 days	234	0	0
Yu, 2012, liver ⁷¹		N	6 months	117 (60/57)	0	0
DhungeI, 2012, heart ⁶⁵		N	6 months	65 (44/21)	2	2
Infection						
Min, 2013 ⁶⁸		Y	6 months	126 (63/63)	10	8
Marfo, 2013, kidney ⁶⁷		N	90 days	73	10	12
Connor, 2012, kidney ⁵⁹		N	6 months	99 (48/51)	4**	4**
DhungeI, 2012, heart ⁶⁰		N	6 months	65 (44/21)	8	1
eGFR (ml/min/1.73m2)						
Min, 2013, kidney ⁶³		Y	6 months	93 (38/55)	66.3 (18.5)	64.4 (16.7)
Rosenborg, 2014, kidney ⁶⁴		N	4 weeks	67	51 (47-55)#	51 (47-55)#
Connor, 2012, kidney ⁶⁴		N	6 months	99 (48/51)	54.3 (20.2)	47.4 (15.2)
Serum creatinine (µmol/L)						
Rosenborg, 2014, kidney ⁶⁹		N	4 weeks	67	129 (118-140)#	131 (119-143)#

Marfo, 2013, kidney ⁶⁷		N	90 days	73	133.48 (48.62)	137.02 (58.34)
Connor, 2012, kidney ⁶⁴		N	6 months	99 (48/51)	127 (111.8-157.2)*	112 (96-167)*
Spence, 2012, kidney, liver, heart ⁷⁰		N	106 days	234	117.57 (42.43)	120.22 (72.49)
Momper, 2011, kidney ⁷³		N	Average 50 days	55	136.14 (68.95)	134.37 (69.84)
Momper, 2011, liver ⁷³		N	Average 50 days	48	142.32 (109.62)	144.09 (116.69)

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mean (95% confidence interval)

*median (IQR)

**CMV disease

I/G, I=Innovator, G=generic

Table C: Cellcept clinical outcomes

Study, year, organ	Definition of acute rejection	Trial (y/n)	Follow up time	Number of patients analyzed (I/G)	Cellcept	Generic
Acute rejection						
Abdallah, 2010, kidney ⁷⁵	Not specified	Y	2 years	18 (10/8)	1	1
Danguilan, 2014, kidney ⁷⁹	Not specified	N	6 months	40 (20/20)	3	1
Rutkowski, 2011, kidney ⁷⁷	Clinical manifestations or biopsy	N	6 months	30 (15/15)	2-clinical 1-biopsy	3-clinical 1-biopsy
Namgoong, 2013, liver ⁷⁶	Not specified	N	3 months	47	0	0
Graft loss						
Danguilan, 2014, kidney ⁷⁹		N	6 months	40 (20/20)	0	0
Death						
Sunder-Plassmann, 2012, kidney ⁷⁸		Y	112 days	43	0	0
Abdallah, 2010, kidney ⁷⁵		Y	2 years	18 (10/8)	0	0
Danguilan, 2014, kidney ⁷⁹		N	6 months	40 (20/20)	0	1
Rutkowski, 2011, kidney ⁷⁷		N	6 months	30 (15/15)	1	1
Infection						
Abdallah, 2010, kidney ⁷⁵		Y	2 years	18 (10/8)	14 (episodes)	9 (episodes)
Danguilan, 2014, kidney ⁷⁹		N	6 months	40 (20/20)	3	5
Rutkowski, 2011, kidney ⁷⁷		N	6 months	30 (15/15)	7	7
eGFR (ml/min/1.73m²)						
Rutkowski, 2011, kidney ⁷⁷		N	6 months	50 (15/15)	58.3	63
Serum creatinine (µmol/L)						
Abdallah, 2010, kidney ⁷⁵		Y	6 months	18 (10/8)	104.48	121.89
Abdallah, 2010, kidney ⁷⁵		Y	1 month	18 (10/8)	202.55	131.06
Videla, 2007, kidney ⁸⁰		N	Before conversion and 60 days post conversion	Unclear	160 (24.75)	134.37 (15.03)
Rutkowski, 2011, kidney ⁷⁷		N	6 months	30 (15/15)	120.22	114.92

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