

## Appendix 2: Characteristics of eligible studies [posted as supplied by author]

Table A: Neoral study characteristics

Study, year	Country	Study Design	Transplant organ	Inclusion Criteria	Exclusion Criteria	Generic	Number of patients (total)	Mean age (Total study or I/G)
Khatami, 2013 <sup>62</sup>	Iran	Randomized parallel group	Kidney	Incident adult transplants	Hyperoxaluria. Primary focal segmental glomerulosclerosis. History of malignancy in the last 5 years. Re-transplant. PRA >25%	Iminoral	221	38.1 (12.6)/39.3 (13.2)
Vitko, 2010 <sup>57</sup>	Czech Republic	Randomized parallel group	Kidney	Transplanted between 1 and 10 years prior to enrollment. Stable graft function. No rejection in the last 6 months. Stable dose of cyclosporine	None specified	Equoral	99	43.4 (11.6)/ 41.1 (12.5)
Qazi, 2006 <sup>47</sup>	USA	Randomized parallel group (10% to Neoral and 90% to Gengraf). Before/after comparisons in Gengraf arm	Kidney	At least 6 months post transplant. Stable graft function. Stable cyclosporine levels	None specified	Gengraf	82	47.5 (5)
Hibberd, 2006 <sup>38</sup>	Australia	Randomized cross over trial	Kidney	Stable transplant recipients. At least 6 months post transplant	None specified	Cysporin	28	53 (10)
David-Neto, 2004 <sup>34</sup>	Brazil	Randomized cross over trial	Kidney	Stable prevalent transplants. Age 18-60. Stable cyclosporine dose	History of active cancer	Zinograf-ME	18	44.7 (12)
First, 1998 <sup>58</sup>	USA	Randomized cross over trial	Kidney	Body weight between 45 to 155 kg. >6 months post transplant. Stable allograft function. No rejection episodes in the last 6 months. No recent change in cyclosporine dose	Multi-organ transplants. Unstable medical problems	Sang-35	32	Not reported
Kim, 1998 <sup>40</sup>	South Korea	Randomized parallel group trial	Kidney	Incident living donor transplants. Adults	None specified	Neoplanta	40	40 (11.9)/ 37.2 (9.3)
Stephan, 1998 <sup>52</sup>	USA	Randomized parallel group trial	Kidney	Incident transplants	None specified	Consupren	36	Not reported
Masri, 1996 <sup>61</sup>	Lebanon	Randomized parallel group trial	Kidney	Prevalent transplants. Unstable Sandimmune pharmacokinetics and Cmax <400 ng/ml. Tmax >3.5 hrs. Broad Cmax. Unstable serum creatinine (>10% variation over 3 measurements)	None specified	Consupren	44	33/32
Fisher, 1999 <sup>59</sup>	USA	Randomized cross over trial	Liver	Stable liver and renal function. More than 1 year post transplant	None specified	SangCya	26	52 (10)
Leet, 2009 <sup>42</sup>	Australia	Randomized cross over trial	Heart	At least 15 months post transplant. Stable dose of cyclosporine. Stable renal function. No rejection in the last 6 months	Comorbidities. Sirolimus use	Cysporin	16	60.06 (8.45)
Toman,	Czech	Randomized parallel group	Heart	At least 6 months post	None specified	Consupren	10	51.2 (12)/ 49.8 (10)

2002 <sup>55</sup>	Republic	trial		transplant. Clinically stable. Stable cyclosporine levels. No significant infection				
Al Wakeel, 2008 <sup>32</sup>	Saudi Arabia/Middle East	Interventional before/after	Kidney	Minimum transplant age of 6 months. Stable graft function	None specified	Sigmasporin Microral	42	37.9 (11.1)
Al Wakeel, 2008 <sup>31</sup>	Saudi Arabia/Middle East	Interventional before/after	Kidney	Minimum transplant age of 6 months. Stable graft function	None specified	Sigmasporin Microral	75	38.9 (10.7)
Sayyah, 2007 <sup>49</sup>	Iran	Interventional before/after	Kidney	Clinically stable for at least 2 months	Severe infections. Liver dysfunction. Malignancy	Iminoral	41	40.12 (13.37)
Masri, 2005 <sup>44</sup>	Turkey, Lebanon, Pakistan	Interventional before/after	Kidney	Prevalent transplants. First transplant. No rejection in the past 6 months	Any of the following within 14 days of study entry: myocardial infarction, condition that might compromise GI tract, liver or kidney function, condition that might influence cyclosporine pharmacokinetics	Equoral	70	33
Fradette, 2005 <sup>37</sup>	Canada	Interventional before/after	Kidney	At least 6 months post transplant. Stable graft function	None specified	Pliva	37	49.2
Perlik, 2005 <sup>46</sup>	Czech Republic	Interventional before/after	Kidney	Stable transplant recipients. No rejection in the past 6 months	Significant co-morbidities. Interacting medications	Equoral	70	Males: 35.3. Females: 34.7
Talaulikar, 2004 <sup>54</sup>	Australia	Interventional before/after	Kidney	More than 3 months post transplant	Liver disease. Instability of graft function. Change of Neoral dose in the last 3 months	Cysporin	40	49.8 (11.4)
Masri, 2004 <sup>43</sup>	Turkey, Pakistan, Lebanon, Czech Republic	Interventional before/after	Kidney	First renal transplant. No rejection in the last 6 months. Stable graft function	Hepatic dysfunction. CMV infection in the last 6 months	Equoral	Not reported	Not reported
Durlik, 2003 <sup>36</sup>	Poland	Interventional before/after	Kidney	At least 6 months post first renal transplant. Stable graft function. On Neoral for at least 3 months. Age 18 to 65 years	None specified	Cicloral	42	42.5
Tsang, 2003 <sup>56</sup>	Hong Kong	Interventional before/after	Kidney	At least 3 months post transplant. On a stable dose of Neoral. No interacting medications. Stable graft function. Age 18-65 years	Conditions or drugs that would alter cyclosporine metabolism and clearance. Pregnancy	Gengraf	20	48.4 (10.7)
Roza, 2002 <sup>48</sup>	USA	Interventional before/after	Kidney	At least 6 months post transplant. Medically stable	Significant medical issues. Taking drugs that influenced cyclosporine metabolism. Pregnancy	Gengraf	50	49.8 (11.4)
Gaston, 1999 <sup>60</sup>	USA	Interventional before/after	Kidney	Stable adult transplant recipients.	None specified	SangCya	32	Not reported
Pamugas, 2012 <sup>45</sup>	Philippines	Prospective cohort	Kidney	Age 18-65 years. Living donor. PRA <10%. Incident transplants	CMV positive donor to CMV negative recipient. Pulmonary TB. Treatment with medications known to interact with cyclosporine	Arpimune	60	38.3 (9.3)/ 36.4 (6)
Diarra, 2010 <sup>35</sup>	Austria	Before/after	Kidney	Stable graft function. Prevalent transplants	None specified	Equoral	59	54 (16)
Kahn, 2010 <sup>39</sup>	South Africa	Retrospective cohort with historical controls (incident	Kidney	Prevalent transplants: stable graft function	None specified	Cicloral	Incident transplant: 49.	Incident transplants: 39.5/ 41.9. Prevalent transplants:

		transplants). Retrospective before/after (prevalent transplants)					Prevalent transplants: 117	Not specified
Spasovski, 2008 <sup>51</sup>	Macedonia	Retrospective cohort	Kidney	Incident living donor recipients. Neoral: 2003. Equoral: 2006	None specified	Equoral	31	38.6 (5.1)/ 39.6 (7.6)
Sharma, 2006 <sup>50</sup>	India	Prospective cohort	Kidney	Incident transplants from November 2003 to March 2005	None specified	Arpimune	37	28.1 (9.5)/ 30.55 (9.8)
Taber, 2005 <sup>53</sup>	USA	Retrospective cohort	Kidney	Incident transplants. Neoral group: Transplanted between January 1999 and May 2001. Gengraf group: transplanted between May 2001 and July 2002	Graft failure within 14 days post transplant. Incomplete data collection	Gengraf	188	48.7/ 51.2
Carnahan, 2003 <sup>33</sup>	USA	Prospective before/after	Kidney	Prevalent transplants	Already taking another generic preparation	Gengraf	46	50.5
Kraeuter, 2013 <sup>41</sup>	Germany	Retrospective before/after	Heart	Clinically stable adult chronic transplant patients transplanted from 1989 to 2009	No rejection episodes at the time of conversion. Lack of patient adherence. Multi-organ transplants	Equoral	20	60.7 (10)

I/G: I=Innovator; G= Generic

Table B: Prograf study characteristics

I/G: I=Innovator; G= Generic

\*Median (range)

Study, year	Country	Study Design	Transplant organ	Inclusion Criteria	Exclusion Criteria	Generic	Number of patients (total)	Mean age (Total study or I/G)
Robertsen, 2014 <sup>74</sup>	Norway	Randomized cross over trial	Kidney	Incident transplants 60 years of age or older	None specified	Tacni	25	69 (60-78)*
Min, 2013 <sup>68</sup>	South Korea	Randomized parallel group trial followed by a crossover trial at 6 months in a subset of patients	Kidney	Adult incident transplant patients (living or deceased)	Kidney from donors after cardiac death. Infection. Liver disease. Previous non renal transplant. Malignancy within 5 years	Tacrobell	126	45.6 (12.4) / 47 (12.7)
Alloway, 2012 <sup>63</sup>	USA	Randomized cross over trial	Kidney	At least 6 months post transplant. On a stable dose of tacrolimus	None specified	Sandoz	71	52 (12.5)
Rosenborg, 2014 <sup>69</sup>	Sweden	Interventional before/after	Kidney	Stable renal function. Inclusion from January to December 2012	New transplants. Active neoplasm	Sandoz	67	57.6 (11)
McDevitt-Potter, 2011 <sup>72</sup>	USA	Interventional before/after	Liver, Kidney, multiorgan	On a stable tacrolimus dose. Prevalent transplants	Changing tacrolimus trough target. Non adherent with monitoring. On a mixture of generic and brand products	Sandoz	70 Liver n=28 Kidney n=27 Multiorgan n=5	52 (12)
Heavner, 2013 <sup>66</sup>	USA	Retrospective cohort	Kidney	Prograf group: admission to hospital from October to December 2009. Generic group: admission from December 2009 to February 2009	Transplant within 90 days of admission. New initiation of tacrolimus	Sandoz	78	51 / 54
Marfo, 2013 <sup>67</sup>	USA	Retrospective before/after and retrospective cohort	Kidney	Switched from brand-name to generic between 2009 and 2010	Less than 3 months post transplant	Any generic	Before/after: 73 Cohort: 106	51 (16) / 54 (13)
Connor, 2012 <sup>64</sup>	United Kingdom	Retrospective cohort	Kidney	Incident transplant patients. Prograf: Transplanted between November 2009 and November 2010. Generic: Transplanted between November 2010 and 2011	None specified	Adoport	99	52 / 57*
Momper, 2011 <sup>73</sup>	USA	Retrospective before/after	Liver, kidney	Liver: at least 6 months post transplant. Kidney: at least 3 months post transplant. Conversion between August 2009 to April 2010	Non adherent with drug level monitoring. Co-prescribed interacting medications	Sandoz	103 Liver: 48 Kidney: 55	Liver: 60.6 (10.9) Kidney: 49.9 (15.1)
Spence, 2012 <sup>70</sup>	USA	Retrospective before/after	Liver, kidney, heart	Clinically stable with conversion to generic between October 1 <sup>st</sup> to December 31 <sup>st</sup> , 2010	None specified	Sandoz	Liver: 29 Kidney: 193 Heart: 12	54 (12.9)
Yu, 2012 <sup>71</sup>	South Korea	Prospective cohort with historical controls	Liver	Incident transplants	Over age 65. Severe infection	Tacrobell	117	51.2 (4.8)/ 48.7 (6.9)
Dhungel, 2013 <sup>65</sup>	USA	Retrospective cohort with historical controls	Heart	Incident transplants	None specified	Generic not specified	65	50.9 (16.5)/ 56.8 (10.2)

Table C: Cellcept study characteristics

Study, year	Country	Study Design	Transplant organ	Inclusion Criteria	Exclusion Criteria	Generic	Number of patients (total)	Mean age (Total study or I/G)
Sunder-Plassmann, 2012 <sup>78</sup>	Multi-centre, International	Randomized cross over trial	Kidney	At least 12 months post transplant. Stable renal function	None specified	Myfenax	43	50.7 (13.5)
Abdallah, 2010 <sup>75</sup>	Tunisia	Randomized parallel group trial	Kidney	All incident transplants between January 2007 and December 2008	None specified	Mycophenolate mofetil 500 (Medis, Tunisia)	18	33.3 (11.7)/ 36.3 (7.1)
Videla, 2007 <sup>80</sup>	Chile	Interventional before/after	Kidney	Stable renal function	None specified	Linfonex	5	Not reported
Danguilan, 2014 <sup>79</sup>	Philippines	Prospective cohort with historical controls	Kidney	18-65 years of age. Incident transplants. Primary kidney transplant from a living donor. PRA <10%	None specified	Mycept	56	Not reported 90% of patients between the ages 20-40
Rutkowski, 2011 <sup>77</sup>	Poland	Cohort	Kidney	Incident transplants from April 2009 to January 2011 (partner kidneys)	None specified	Myfenax	15	49/54.1
Namgoong, 2013 <sup>76</sup>	South Korea	Prospective before/after	Liver	Transplant 2 years or more before the study with stable function	None specified	Myconol	53	55.9 (7.1)

I/G: I=Innovator; G= Generic