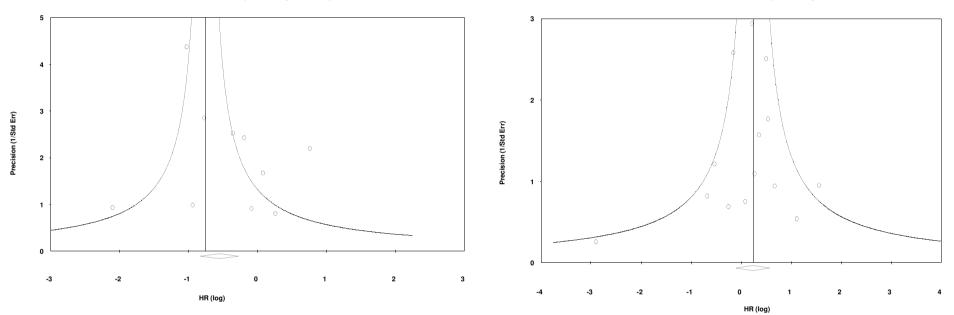
Appendix 2: Supplementary figures A-F

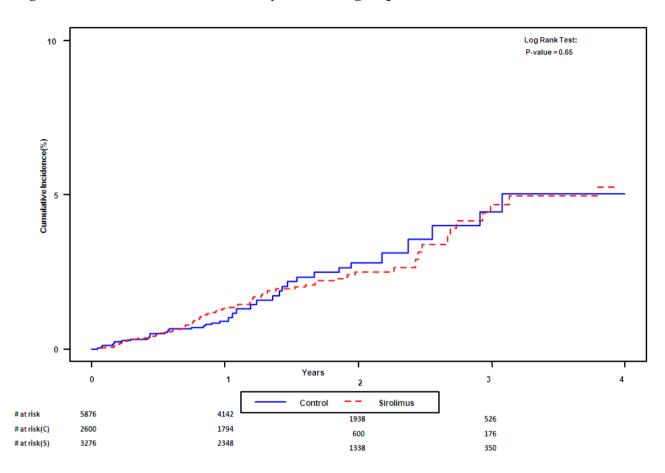
Figure A: Funnel plots for cancer and death



Funnel Plot of Precision by HR (log) for Any Cancer

Funnel Plot of Precision by HR (log) for Death

Figure B. Time to first other cancer by treatment group*

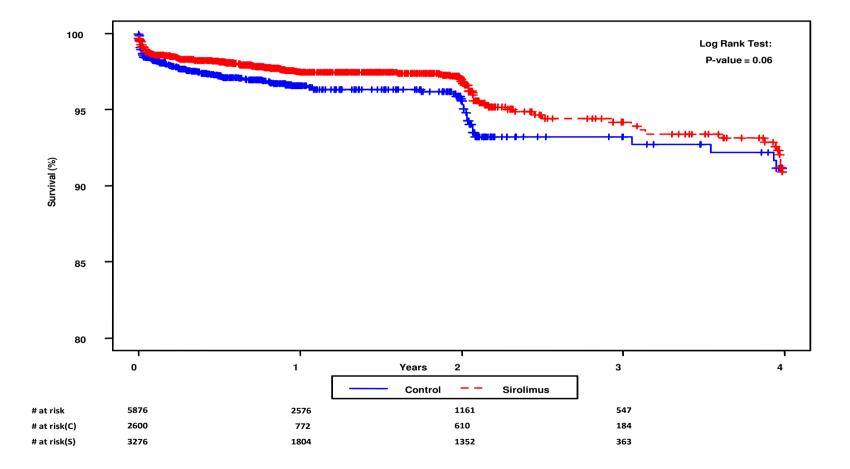


*Includes all cancers but basal cell and squamous cell skin cancer

Figure C: Plot of mortality grouped by de novo and conversion trial

Study	Events	Patients	HR (95%CI)	Hazard Ratio
De NOVO trials				I
Barsoum 2007	6	113	0.59 (0.12, 2.98)	_
Ekberg 2007	43	1589	1.25 (0.64, 2.44)	
Flechner 2011	20	443	1.73 (0.57, 5.26)	
Gallon 2006	2	82		
Gelens 2006	1	54		
Glotz 2010	5	141	1.32 (0.22, 7.94)	=
Groth 1999	0	83		
Kahan 1999	9	149	1.97 (0.24, 15.88)	_
Kahan 2000	19	719	1.44 (0.41, 5.03)	_
Kreis 2000	3	78	0.51 (0.05, 5.67)	e
MacDonald 2001	36	575	0.86 (0.40, 1.84)	_
Machado 2004	2	70	0.78 (0.04, 13.52)	_
Sampaio 2008	3	98	1.09 (0.08, 14.94)	e
Flechner 2013	10	475	4.77 (0.60, 37.71)	
Vitko 2006	0	48		
Conversion trials				
Blydt-Hansen 2010	0	22		
Campbell 2012	2	86	3.07 (0.08, 118.34)	-
Guba 2010	2	140	0.06 (0.00, 124.44)	<u> </u>
Salgo 2010	0	44		
Schena 2009	39	829	1.66 (0.76, 3.63)	
Watson 2005	0	38		
Overall	202	5876	1.43(1.21,1.71)	





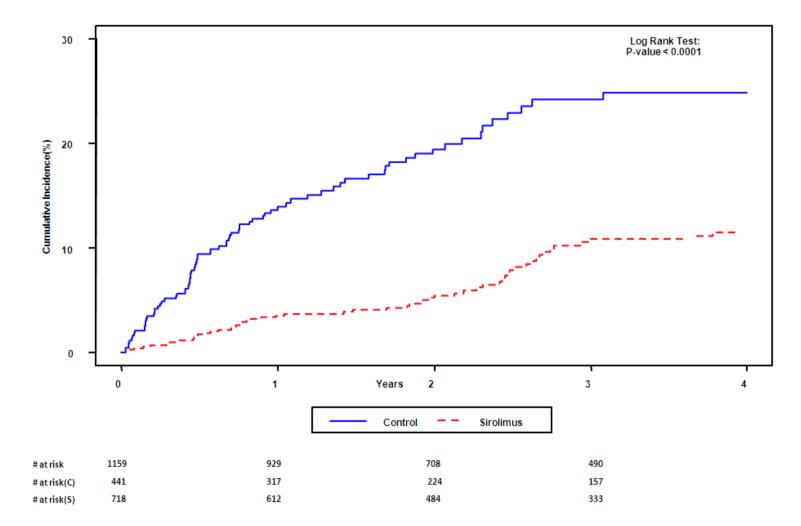


Figure E: Time to first malignancy for patients in conversion trials by treatment group

Figure F: Risk of outcomes in sirolimus versus control patients – supplementary subgroup analyses*

					Tiazara Tiatio
Any Cancer	Trials	Events	Patients	HR (95%CI)	
Induction	8	41	2467	1.26 (0.61, 2.61)	-
No Induction	15	84	2492	0.68 (0.45, 1.01)	
Living Donor	17	62	2023	0.65 (0.36, 1.17)	-
Deceased Donor	18	173	3806	0.64 (0.41, 0.99)	
Non-Melanoma Skin cancer					
Induction	8	14	2467	1.42 (0.49, 4.14)	
No Induction	15	48	2492	0.35 (0.22, 0.55)	-
Living Donor	17	39	2023	0.45 (0.23, 0.87)	
Deceased Donor	18	103	3806	0.47 (0.36, 0.63)	
Other Cancer					
Induction	8	28	2467	1.25 (0.39, 3.98)	
No Induction	15	39	2492	1.82 (1.25, 2.65)	
Living Donor	17	25	2023	1.47 (0.92, 2.36)	
Deceased Donor	18	81	3806	0.93 (0.43, 2.02)	
Death					
Induction	8	68	2467	1.90 (1.36, 2.68)	
No Induction	15	93	2492	1.02 (0.77, 1.34)	_ -
Living Donor	17	33	2023	1.00 (0.56, 1.78)	
Deceased Donor	18	169	3806	1.52 (1.21, 1.91)	_
					0.2 0.5 1.0 2.0 5
					0.2 0.5 1.0 2.0 5 Favours Sirolimus Favours Control

* These analyses should be interpreted with caution as they are subgroups from trials designed to evaluate sirolimus; patients were not randomized to treatment groups based on induction/no induction or deceased/living donor and may be imbalanced for other factors associated with cancer or death. In addition, 3 trials had missing data on induction therapy and 3 trials had missing data on donor type.

Hazard Ratio