

**Table 2.1. Cohort studies and meta-analysis of ciclosporin and cancer risk**

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/deaths	Relative risk (95%CI)*	Adjustment for potential confounders	Comments	
Väkevä et al. (2008) Helsinki, Finland	Cohort of 272 (116 men and 156 women) inflammatory skin disorders (psoriasis, dermatitis, eczema) patients treated with CsA. Age 17–76 yr, median age 38 yr; patients with prior malignancy were excluded		Skin	Overall	236	1.31 (0.70–2.23)	Age, gender, CsA dose, methotrexate, phototherapy use	No analysis of cumulative dose; point estimates and number of cases not reported for low or high dose	
				Medium: 2–4 mg/kg	11	1.34 (0.37–4.39)			
				Lymphoma	Men	NR			1.91
				Women	NR	0.96			
				Age: Males > 45 yr	NR	3.28 (1.06–7.64)			
Grulich et al. (2007) Australia, Canada, Denmark, Finland, Sweden Studies included in the meta-analysis: Kyllönen et al. (2000), Birkeland et al. (2000), Adami et al. (2003), Vajdic et al. (2006), Villeneuve et al. (2007)	Meta-analysis of log standardized incidence comparing immunosuppressed patients. 31977 transplant recipients from Australia, Canada, Denmark, Finland and Sweden from the period between 1964–2003		All Cancers	Overall	3125	3.33 (2.92–3.79)		Pubmed based meta-analysis. No subset analysis of calcineurin inhibitor used. No comment on induction	
				Oral cavity and pharynx		49			3.23 (2.40–4.35)
				Non-melanoma skin		448			28.62 (9.39–87.2)
				Non-Hodgkin lymphoma		333			8.07 (6.40–10.2)

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Kessler et al. (2006) Nancy, France	Retrospective cohort analysis of 488 renal transplant recipients treated with CsA between 1985–95. Mean age at transplant was 42 yr		All Cancers	<i>Men</i>	38	2.2 (1.5–3.0)	Age, gender	Reference population, French Cancer Registry (FRANCIM)
				<i>Women</i>	21	3.0 (1.9–4.6)		
			PTLD	<i>Men</i>	NR	9.5 (3.1–22.1)		
				<i>Women</i>	NR	28.9 (9.4–67.6)		
			Kidney	<i>Men</i>	7	13 (5.2–26.8)		
				<i>Women</i>	4	35.2 (9.6–90.1)		
				Cervix	6	25.3 (9.3–55.0)		
			Kasiske et al. (2004) Minneapolis, USA	Retrospective cohort analysis of 35765 renal transplant recipients identified through Medicare billing claims for renal transplant and in- or out- patient cancer care between 1995–2001		Non-Hodgkin lymphoma		
Melanoma		NR				2.19 (1.31–3.65)		
Kidney		NR				1.39 (1.10–1.76)		
Skin		NR				2.55 (2.26–2.88)		

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Bustami et al. (2004) Michigan, USA	Retrospective cohort analysis of 41000 first-time cadaveric transplant recipients transplanted after 1995 and followed through 2002 identified through the Organ Procurement and Transplantation Network. 55% of these patients did not receive induction therapy. 55.7% of the induction and non-induction patients received CsA		Any non-skin		NR	1.17 (1.07–1.28)				
				Skin	CsA	NR	1.02 (0.86–2.21)			
					Microemulsion CsA	NR	1.01 (0.86–1.18)			
			Non-skin	CsA	NR	1.0 (0.86–1.18)				
				Microemulsion CsA	NR	0.98 (0.85–1.13)				
			PTLD				181			
				Induction (ATG)				1.50 (0.93–2.43)		
				CsA vs Tac	NR			1.12 (P = 0.64)		
				No Induction CsA vs Tac	NR			2.03 (P < 0.008)		
			de novo solid cancers				616			
Induction (ATG)					1.24 (0.97–1.58)					
CsA vs Tac	NR				1.16					

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						(P = 0.38)		
				<i>No Induction</i>				
				<i>CsA vs Tac</i>	NR	0.7 (P = 0.02)		
Opelz & Döhler (2004) Heidelberg, Germany	Retrospective cohort analysis of 145104 cadaveric renal transplants followed between 1985 and 2001 from the Collaborative Transplant Study Database		Lymphoma	<i>Lymphoma</i>		11.8 (11.0–12.6)	Age, gender, geography	
				<i>1<sup>st</sup> Transplant</i>	124 473	11.7		
				<i>2<sup>nd</sup> Transplant</i>	20 631	12.1		
				<i>CsA+ steroids +/-Aza</i>		12.7		
				<i>Steroids + Aza</i>		14.3		
				<i>Dose Effect of CsA</i>		P = NS		

ATG, antithymocyte globulin; Aza, azathioprine; CsA, ciclosporin; ESRD, end-stage renal disease; NR, not reported; NS, not significant; PTLD, post-transplant lymphoproliferative disorder; Tac, tacrolimus; vs, versus; yr, year or years