



Immunosuppression Rejktion

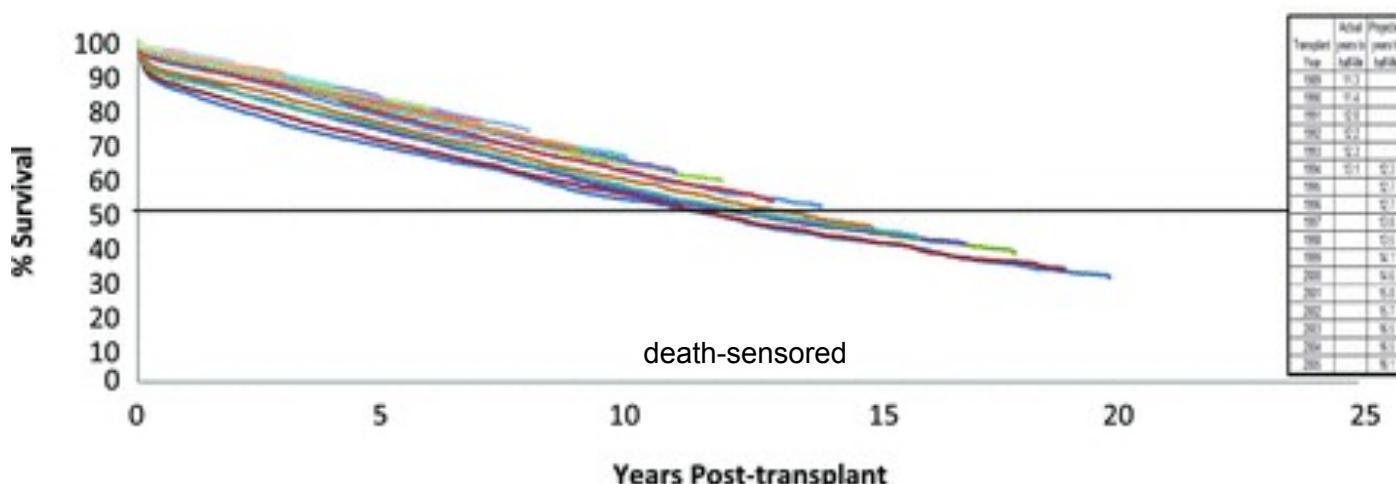
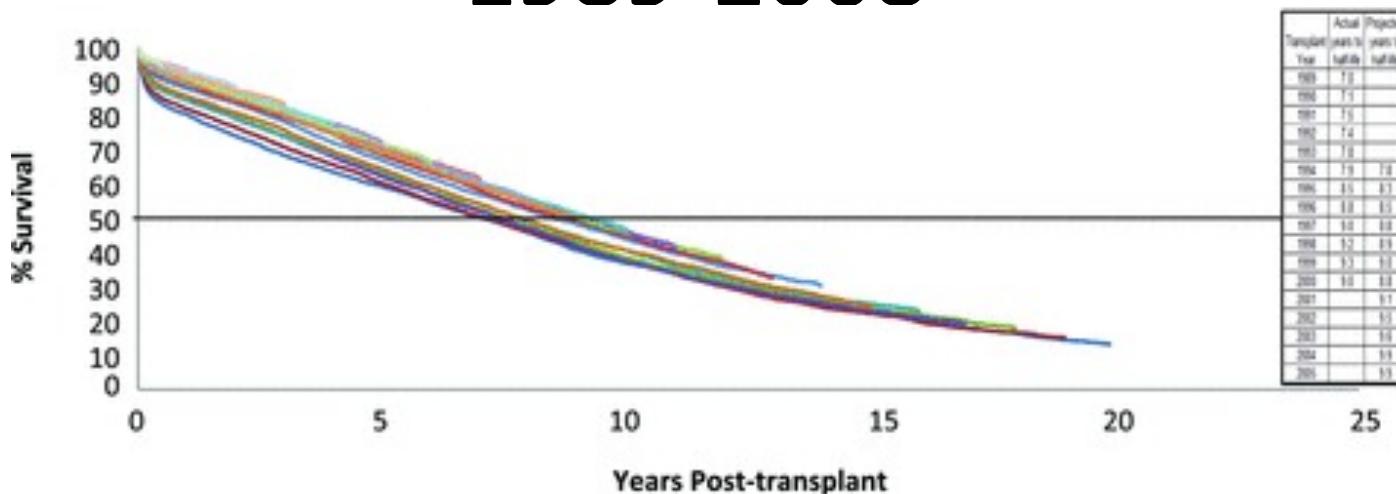
Nefroseminariet
Bosön
161025

Jana Ekberg

Transplantationscentrum
Sahlgrenska Universitetssjukhuset
Göteborg

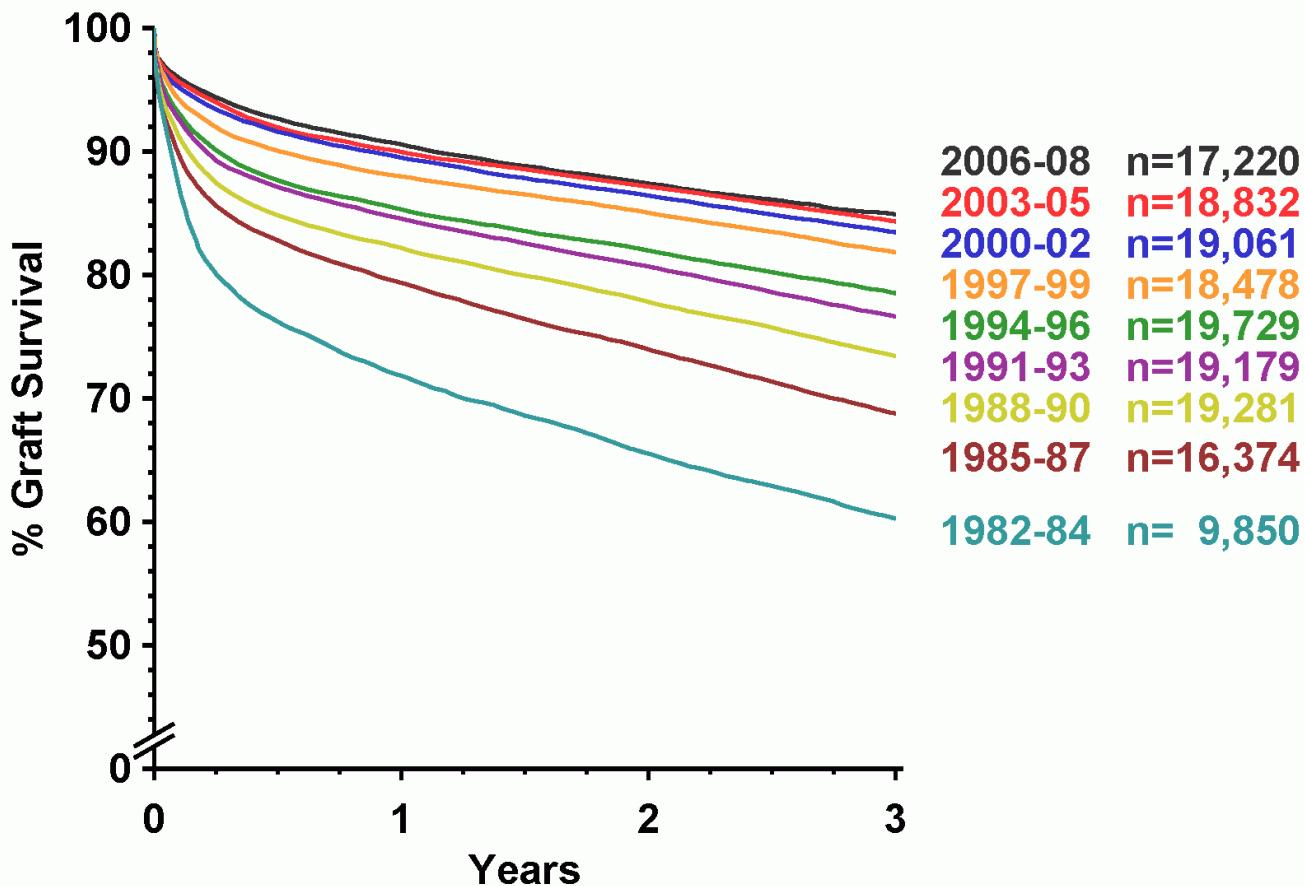


Graft survival , 1 st TX, SCD, 1989-2008

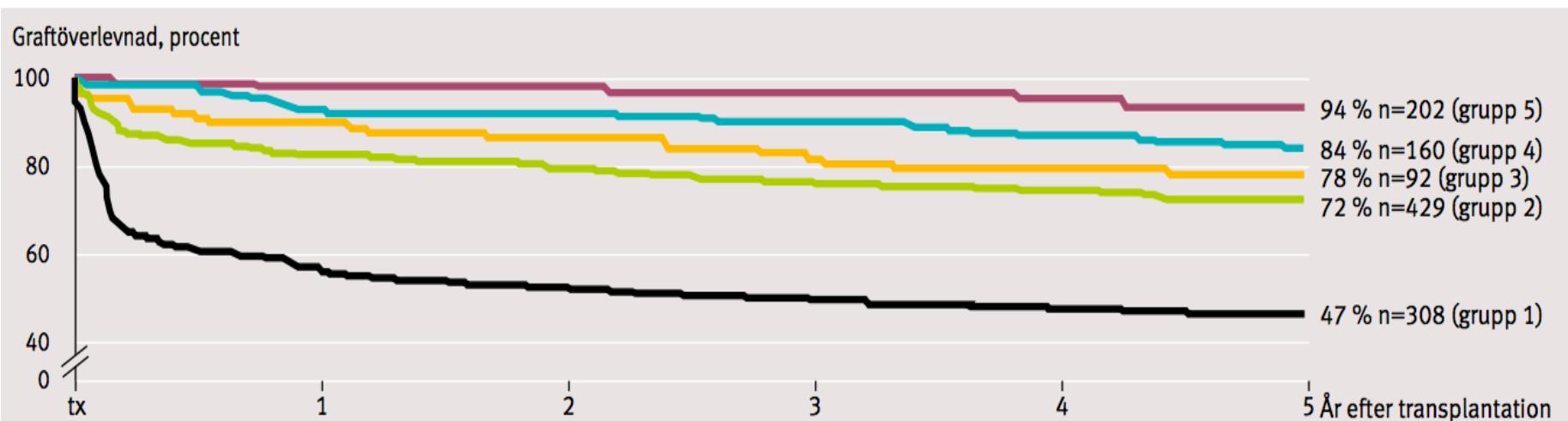


Transplant Year

Deceased Donor, First Kidney Transplants Europe



Graftöverlevnad, olika tidsperioder, Sverige



Grupp	Tidsperiod	Immunsuppressiv behandling ¹	Akut rejktion, procent	5 års graftöverlevnad, procent
1	1969–1982	Azatioprin + prednisolon	? ²	47
2	1983–1995	Ciklosporin + azatioprin + prednisolon	60	72
3	1996–1998	Ciklosporin + mykofenolatmofetil + prednisolon	41	78
4	1999–2004	Takrolimus + mykofenolatmofetil + prednisolon	32	84
5	2005–2010	Lågdos takrolimus + mykofenolatmofetil + prednisolon	10	94

¹ Under de två senare tidsperioderna (sedan 1999) har även ingått induktionsbehandling med monoklonal antikropp mot T-lymfocytens interleukin-2-receptor (först daclizumab som numera utgått, senare basiliximab; enstaka doser vid transplantationstillfället).

² Data avseende akut rejktion för denna tidsperiod saknas.

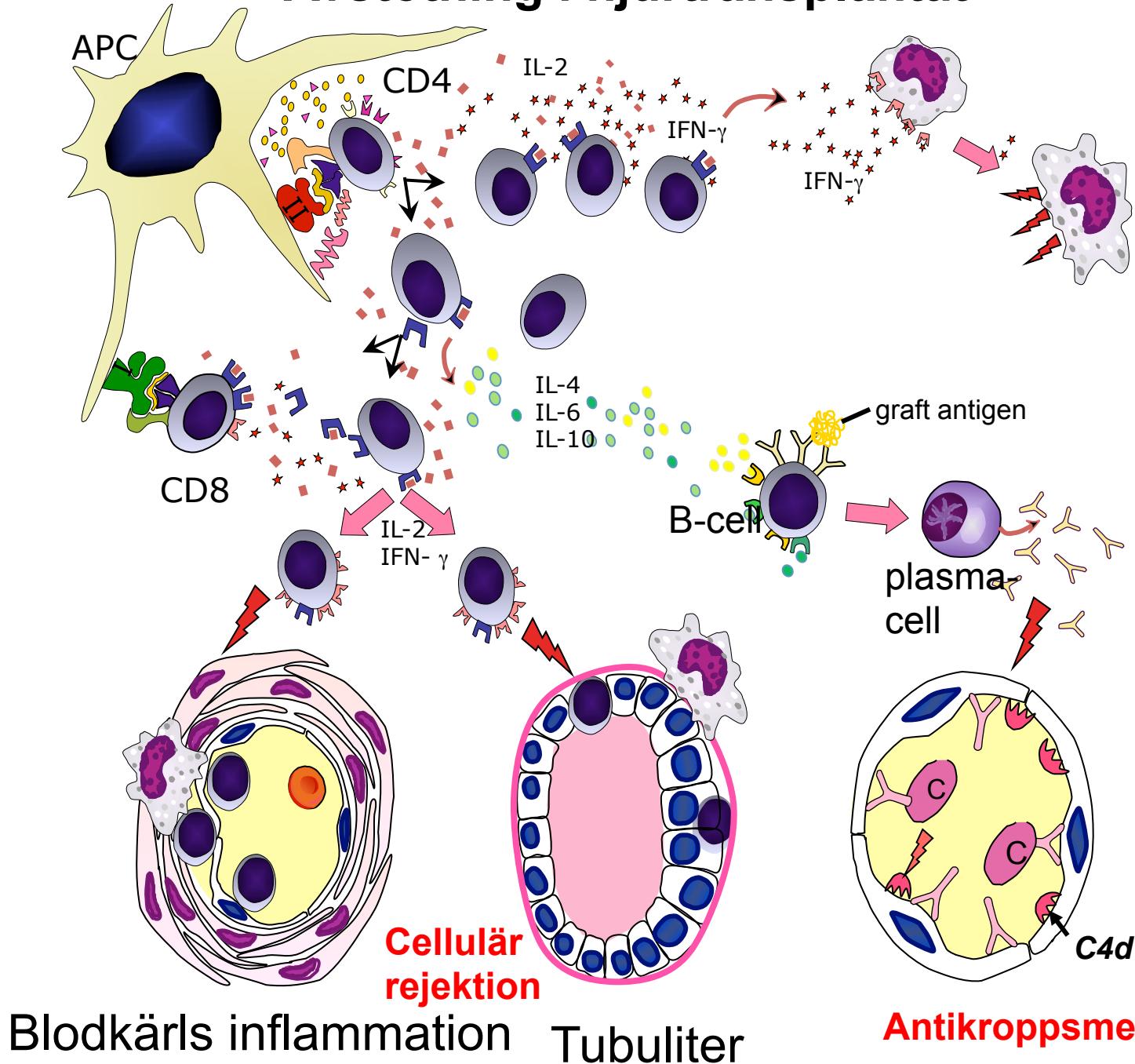
Immunosuppression

Historik

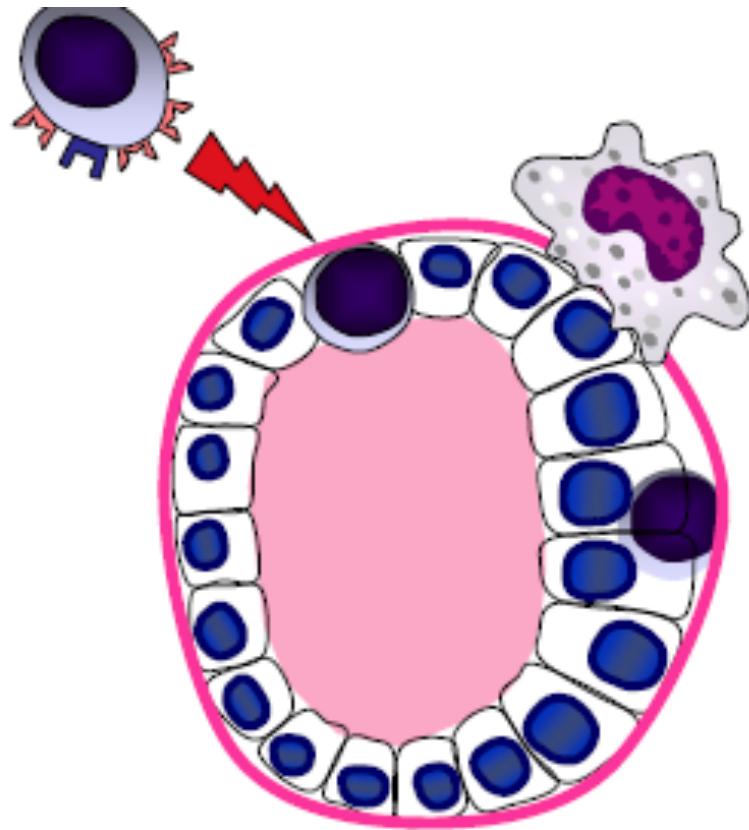
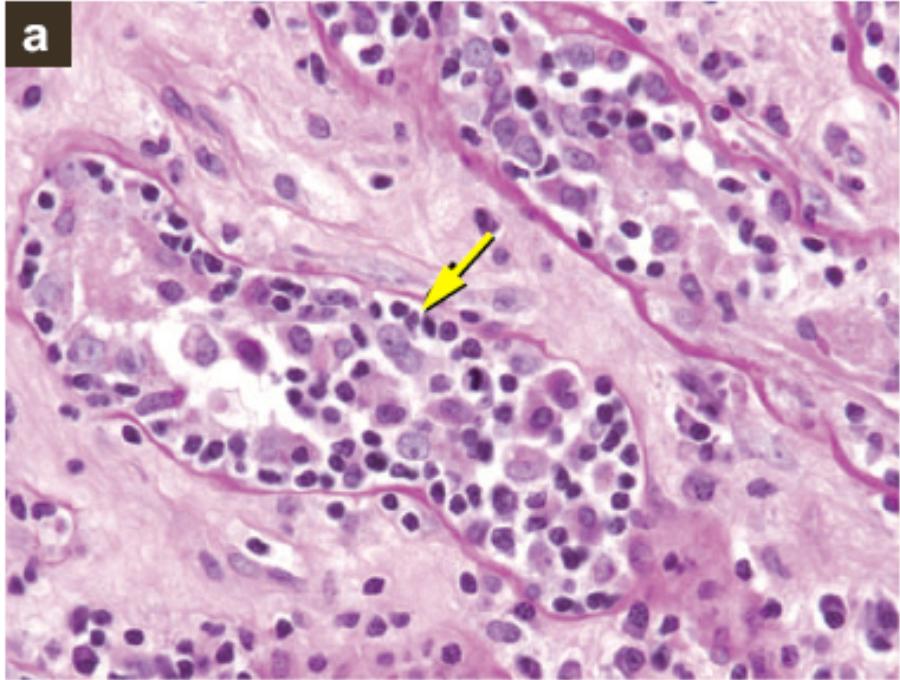
1950-tal Helkropps- bestrålning	1960-tal Anti Thymocyt Globulin (i.v.)	1990-tal Takrolimus Prograf ®	2000-tal mTOR sirolimus (Rapamune®) everolimus(Certican®) anti-IL2R
1950-tal Kortison Azathioprin (Imurel ®)	1980-tal Cyklosporin A Sandimmun ®	1990-tal Mycofenolatsyra “MMF” CellCept ® /Myfortic ®	2010-tal Belatacept Rituximab Bortezomib Eculizumab - IdeS?



Avstötning i njurtransplantat



Tubulit

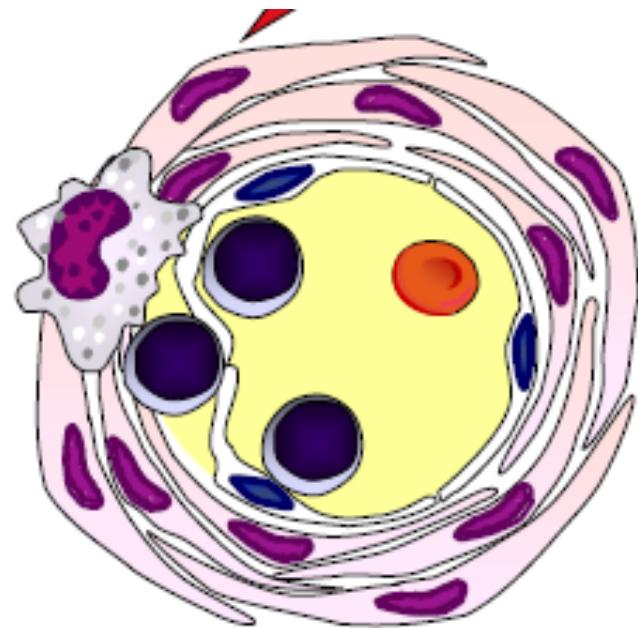
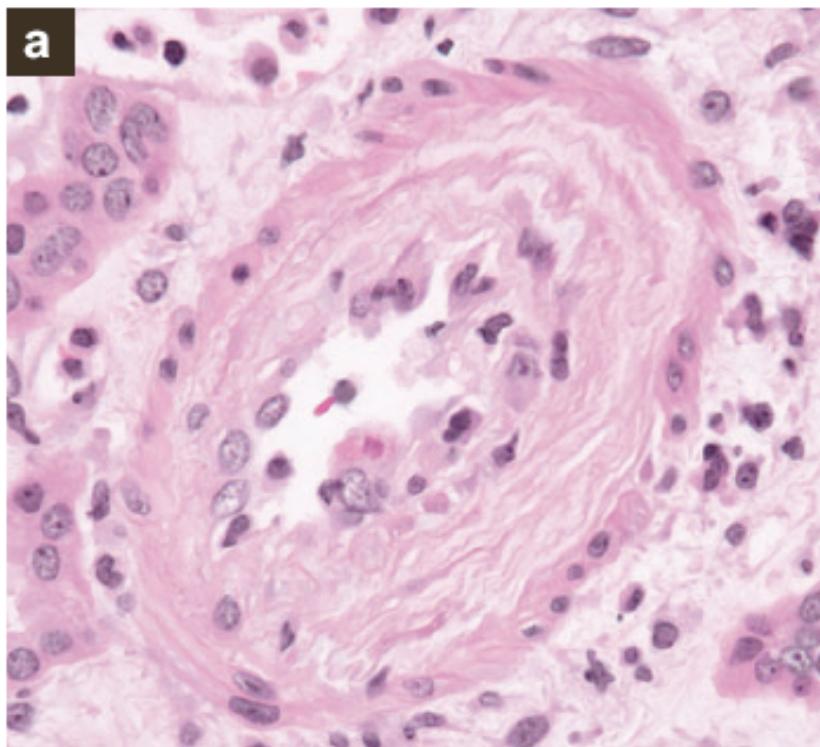


Tubulit

Cornell LD Annu Rev Pathol. 2008;3:189-220.

J Mölne

Vaskulit



Endarterit

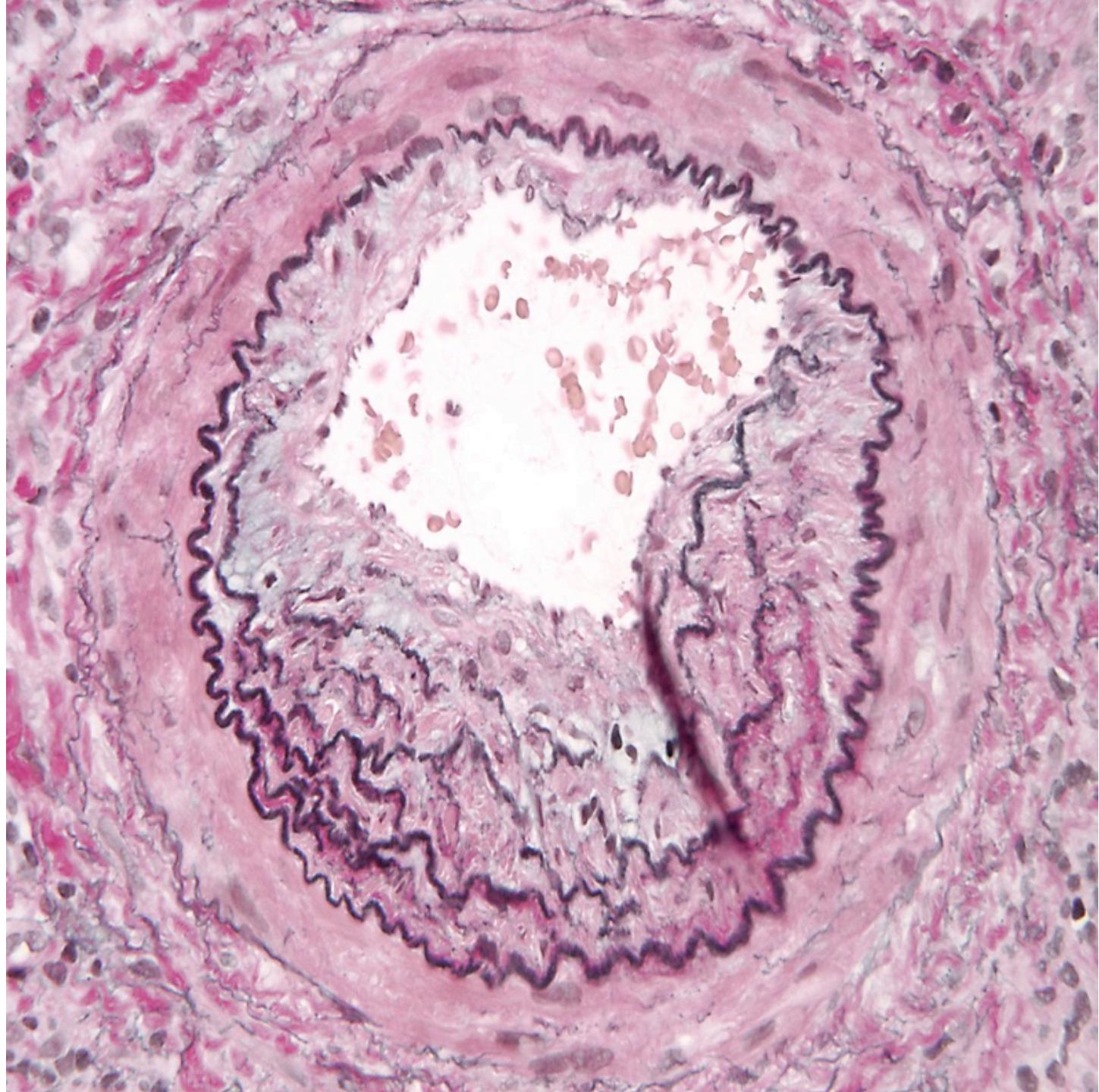


Table 3: Banff 97 diagnostic categories for renal allograft biopsies—Banff'07 update^{1,2}

1. Normal

2. Antibody-mediated changes (may coincide with categories 3, 4 and 5 and 6)

Due to documentation of circulating antidonor antibody, and C4d³ or allograft pathology

C4d deposition without morphologic evidence of active rejection

C4d+, presence of circulating antidonor antibodies, no signs of acute or chronic TCMR or ABMR (i.e. g0, cg0, ptc0, no ptc lamination). Cases with simultaneous borderline changes or ATN are considered as indeterminate

Acute antibody-mediated rejection⁴

C4d+, presence of circulating antidonor antibodies, morphologic evidence of acute tissue injury, such as (Type/Grade):

I. ATN-like minimal inflammation

II. Capillary and/or glomerular inflammation ($\text{ptc/g} > 0$) and/or thromboses

III. Arterial—v3

Chronic active antibody-mediated rejection⁴

C4d+, presence of circulating antidonor antibodies, morphologic evidence of chronic tissue injury, such as glomerular double contours and/or peritubular capillary basement membrane multilayering and/or interstitial fibrosis/tubular atrophy and/or fibrous intimal thickening in arteries

3. Borderline changes: 'Suspicious' for acute T-cell-mediated rejection (may coincide with categories 2 and 5 and 6)

This category is used when no intimal arteritis is present, but there are foci of tubulitis (t1, t2 or t3) with minor interstitial infiltration (i0 or i1) or interstitial infiltration (i2, i3) with mild (t1) tubulitis

4. T-cell-mediated rejection (TCMR, may coincide with categories 2 and 5 and 6)

Acute T-cell-mediated rejection (Type/Grade):

IA. Cases with significant interstitial infiltration (>25% of parenchyma affected, i2 or i3) and foci of moderate tubulitis (t2)

IB. Cases with significant interstitial infiltration (>25% of parenchyma affected, i2 or i3) and foci of severe tubulitis (t3)

IIA. Cases with mild-to-moderate intimal arteritis (v1)

IIIB. Cases with severe intimal arteritis comprising >25% of the luminal area (v2)

III. Cases with 'transmural' arteritis and/or arterial fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocytic inflammation (v3)

Chronic active T-cell-mediated rejection

'chronic allograft arteriopathy' (arterial intimal fibrosis with mononuclear cell infiltration in fibrosis, formation of neo-intima)

5. Interstitial fibrosis and tubular atrophy, no evidence of any specific etiology

(may include nonspecific vascular and glomerular sclerosis, but severity graded by tubulointerstitial features)

Grade

I. Mild interstitial fibrosis and tubular atrophy (<25% of cortical area)

II. Moderate interstitial fibrosis and tubular atrophy (26–50% of cortical area)

III. Severe interstitial fibrosis and tubular atrophy/ loss (>50% of cortical area)

6. Other: Changes not considered to be due to rejection—acute and/or chronic (for diagnoses see Table 14 in (42); may include isolated g, cg or cv lesions and coincide with categories 2, 3, 4 and 5)

Cardiovascular risk factors associated with immunosuppression in renal transplantation¹

[Bertram L. Kasiske](#)  [Christie M. Ballantyne](#)

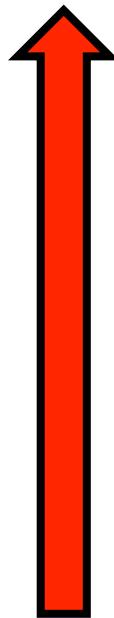
Transplantation Reviews



Cancer after Kidney Transplantation in the United States

AJT, 2004

Bertram L. Kasiske^{a,b,c,*}, Jon J. Snyder^c, David T. Gilbertson^c and Changchun Wang^c



non-melanom hudca
lymfom
njurca
melanom
hepatobiliärca
cervix/vulvaca
testisca
blåsca



Diabetes Mellitus after Kidney Transplantation in the United States

AJT, 2002

Bertram L. Kasiske^{a,b,*}, Jon J. Snyder^a, David
Gilbertson^a and Arthur J. Matas^{a,c}

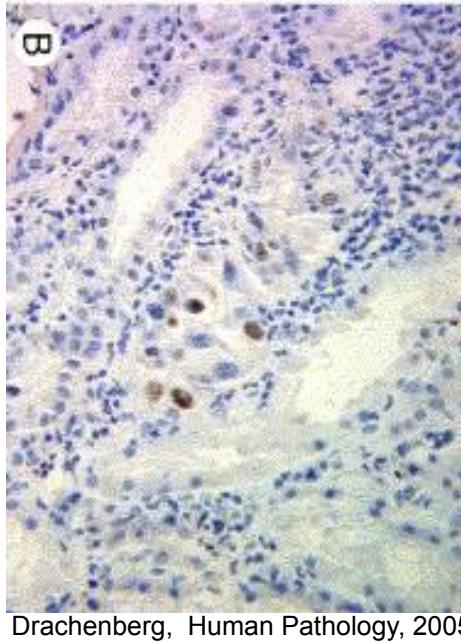
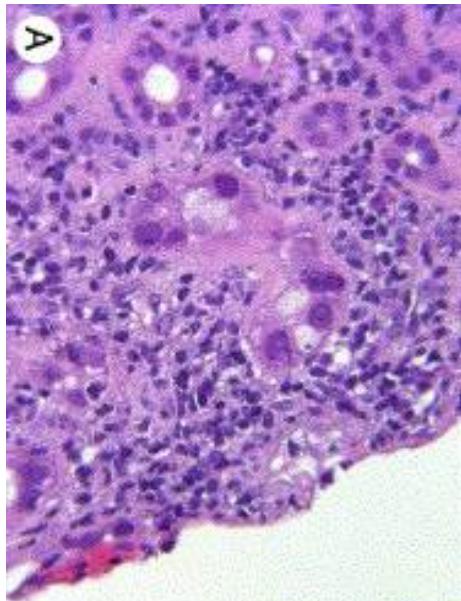
1-y incidens 16%

↑ graftförlust

↓ mortalitet

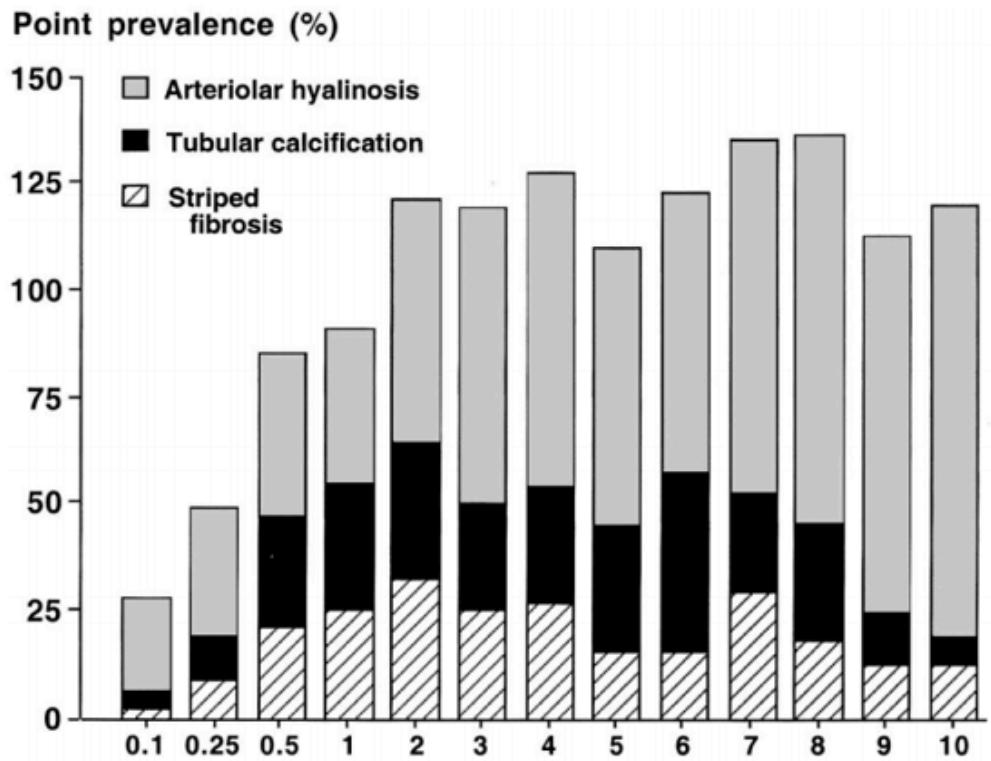


Oportunistisk infektioner Polyomavirus - BKV



Calcineurin Inhibitor Nephrotoxicity: Longitudinal Assessment by Protocol Histology

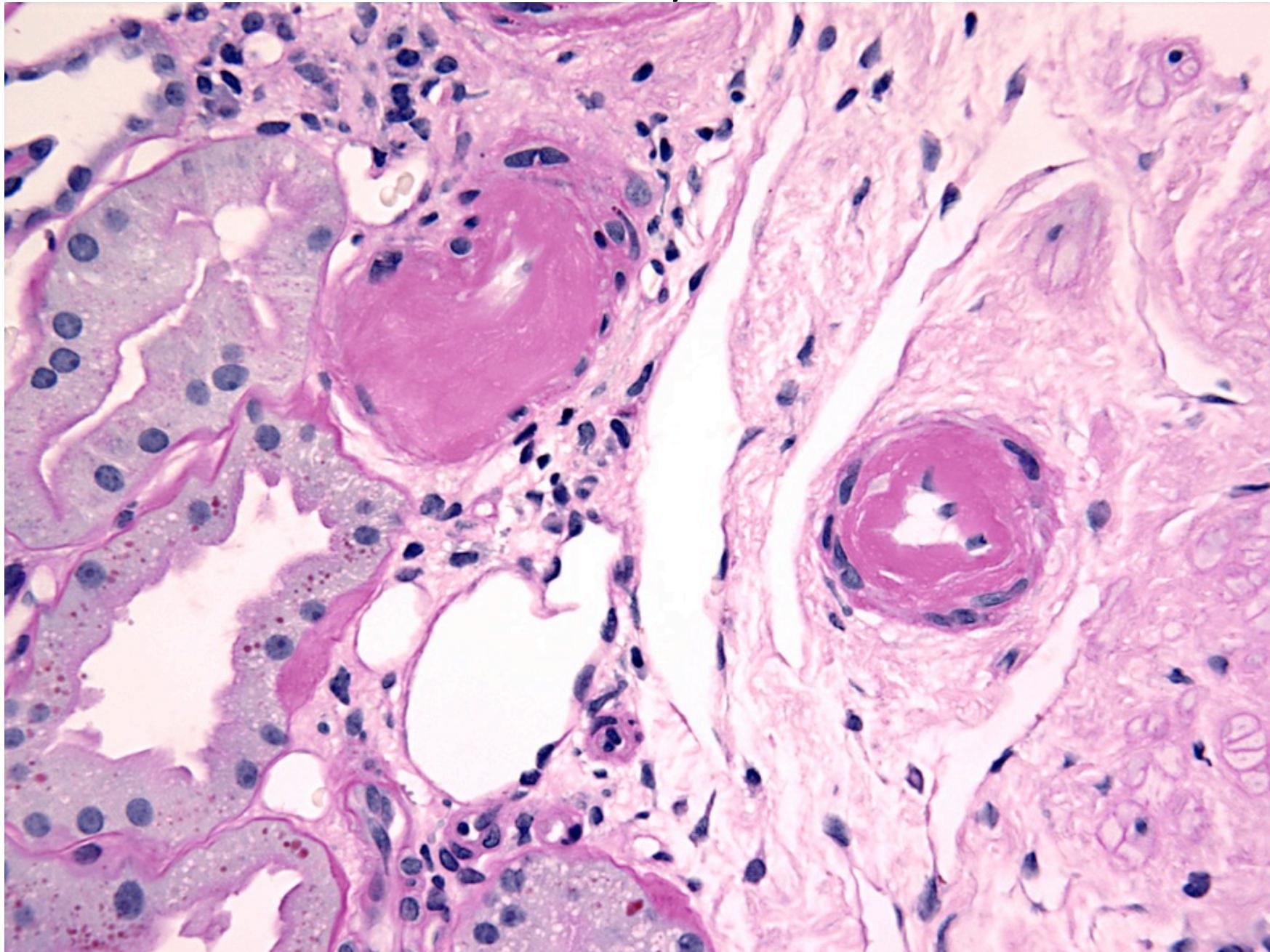
Brian J. Nankivell,^{1,5} Richard J. Borrows,^{1,2} Caroline L.-S. Fung,³ Philip J. O'Connell,¹
Jeremy R. Chapman,¹ and Richard D. M. Allen⁴



Transplantation, 2004



Arteriolohyalinos



Steroid-sparing strategies

Cochrane review

- No effect on mortality or graft loss
- AR more frequent
- Lower incidence of NODAT
- Less cardiovascular events
- Benefit to blood pressure / lipid control

Pascual, The Cochrane Collaboration, 2009

Cyclosporine Sparing with Mycophenolate Mofetil, Daclizumab and Corticosteroids in Renal Allograft Recipients: The CAESAR Study

H. Ekberg^{a,*}, J. Grinyó^b, B. Nashan^c,
Y. Vanrenterghem^d, F. Vincenti^e, A. Voulgaris^f,
M. Truman^g, C. Nasmyth-Miller^f and
M. Rashford^f on behalf of the CAESAR
study group

RCT
n=523
anti-IL2R som induktion
MMF, Prednisolon

- 1.CyA utsättning m 6
- 2.Låg CyA
- 3.Standart CyA

