

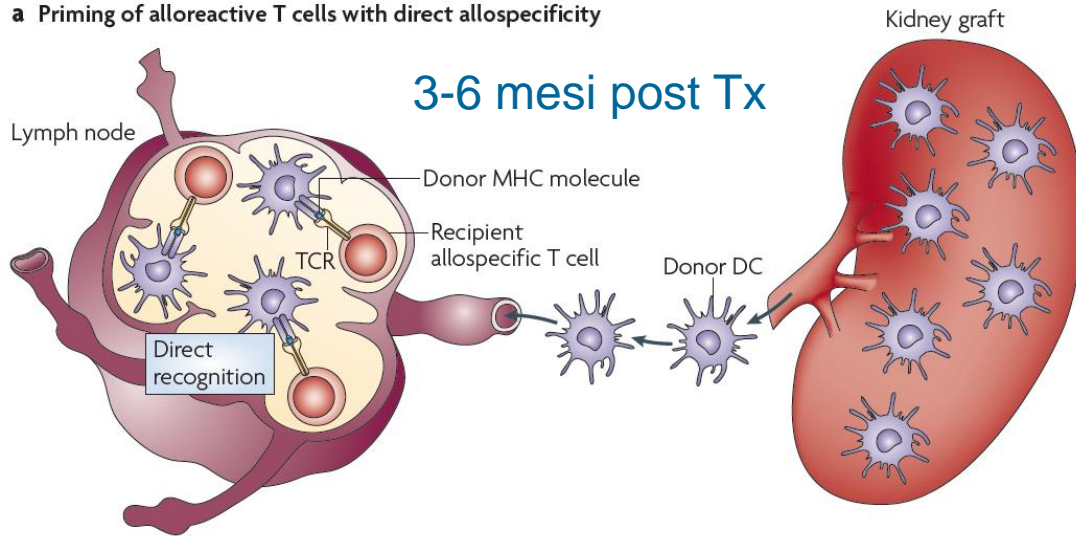
# **Aspetti medici importanti della presa a carico post-trapianto**

16.10.2010

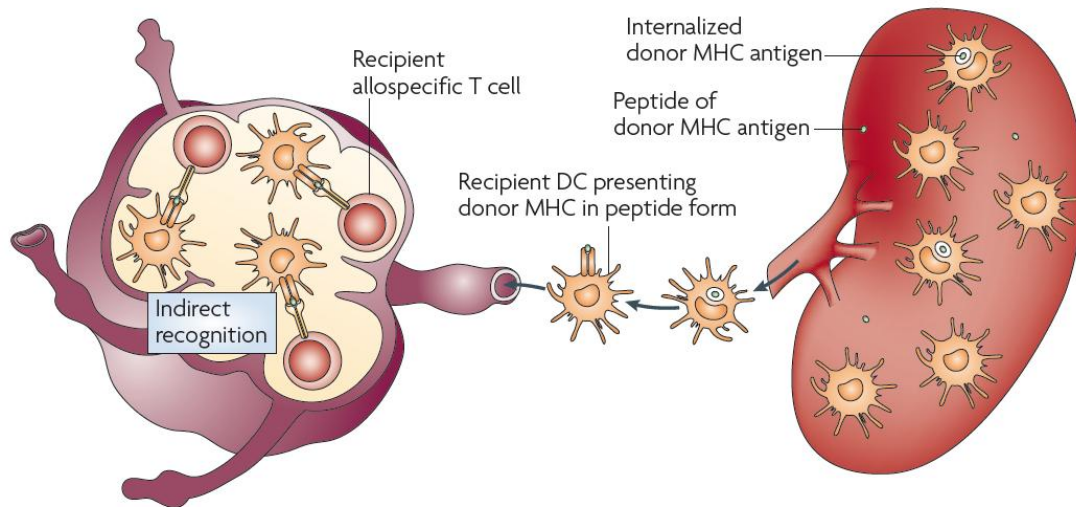
Dr. med. Massimiliano Fontana



**a** Priming of alloreactive T cells with direct allospecificity



**b** Late phase post-transplantation

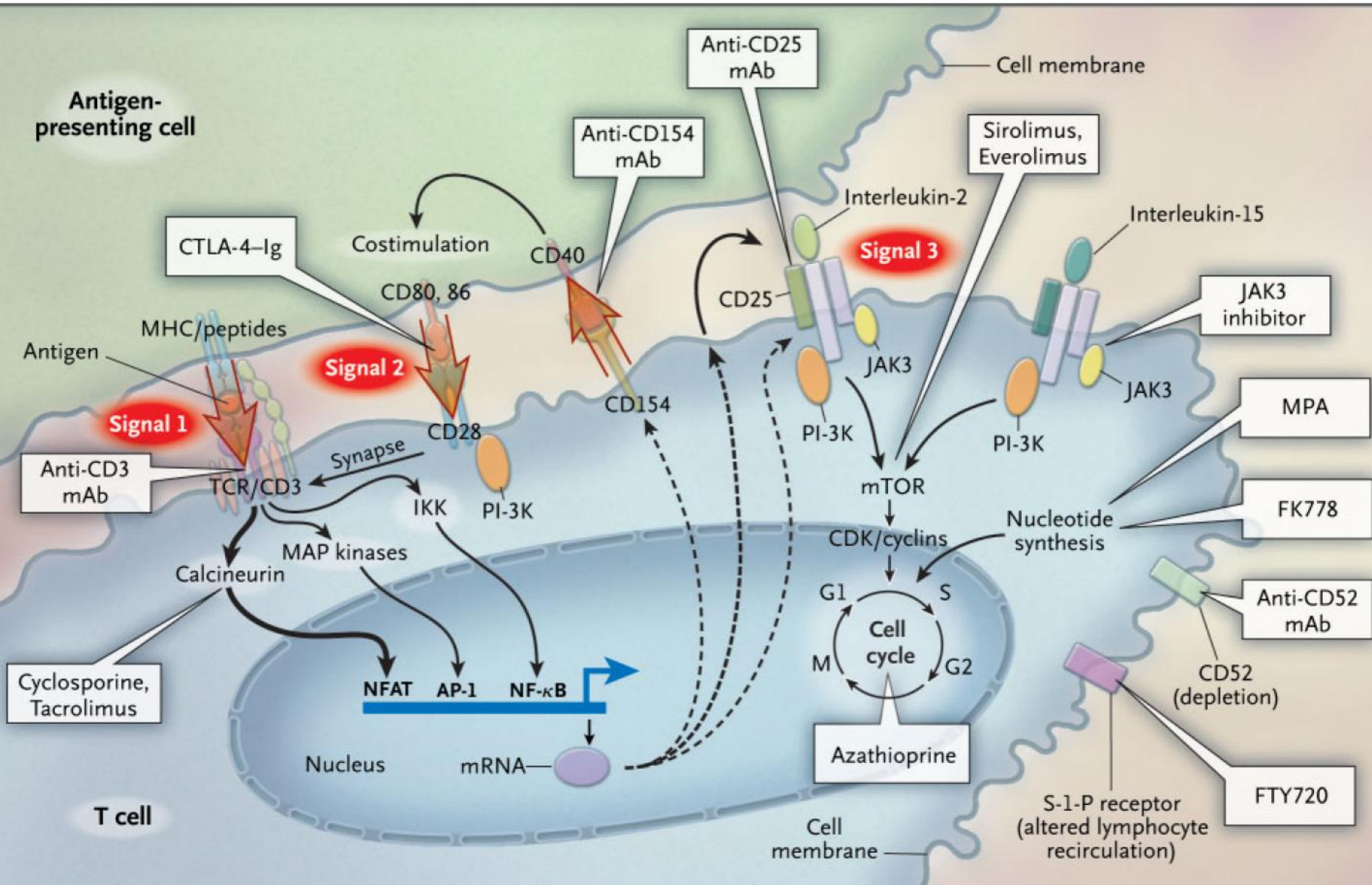


Turka LA, Lechler RI

Nature Reviews Immunology  
July 2009

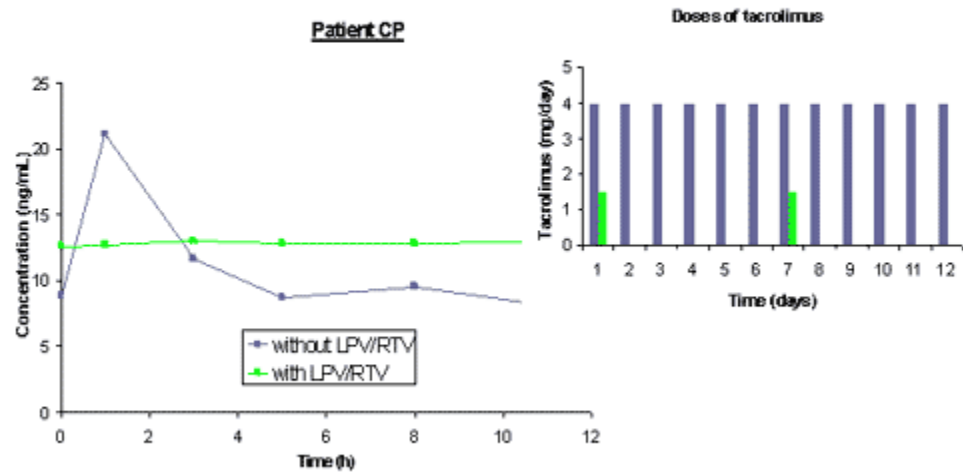
Figure 1 | **Immune response to transplanted organs and tissues.** **a** | The initial site of encounter of foreign MHC molecules occurs in secondary lymphoid tissues, not in the allograft. Shortly after engraftment, donor dendritic cells (DCs) that reside in the transplanted organs and/or tissues migrate to regional lymph nodes, where they activate host T cells. This response is mediated through the direct recognition of intact donor MHC molecules on the surface of DCs by recipient T cells. **b** | During late phase post-transplantation, indirect allorecognition predominates. Recipient DCs circulate into the graft and internalize donor MHC antigen that is shed by allograft cells. These DCs then circulate into regional lymphoid tissues, where they present the processed donor antigens on self MHC molecules to recipient T cells.





**Figure 2. Individual Immunosuppressive Drugs and Sites of Action in the Three-Signal Model.**

Anti-CD154 antibody has been withdrawn from clinical trials but remains of interest. FTY720 engagement of sphingosine-1-phosphate (S-1-P) receptors triggers and internalizes the receptors and alters lymphocyte recirculation, causing lymphopenia. Antagonists of chemokine receptors (not shown) are also being developed in preclinical models. MPA denotes mycophenolic acid.



## Prevalence of anti-HLA antibodies after liver transplantation

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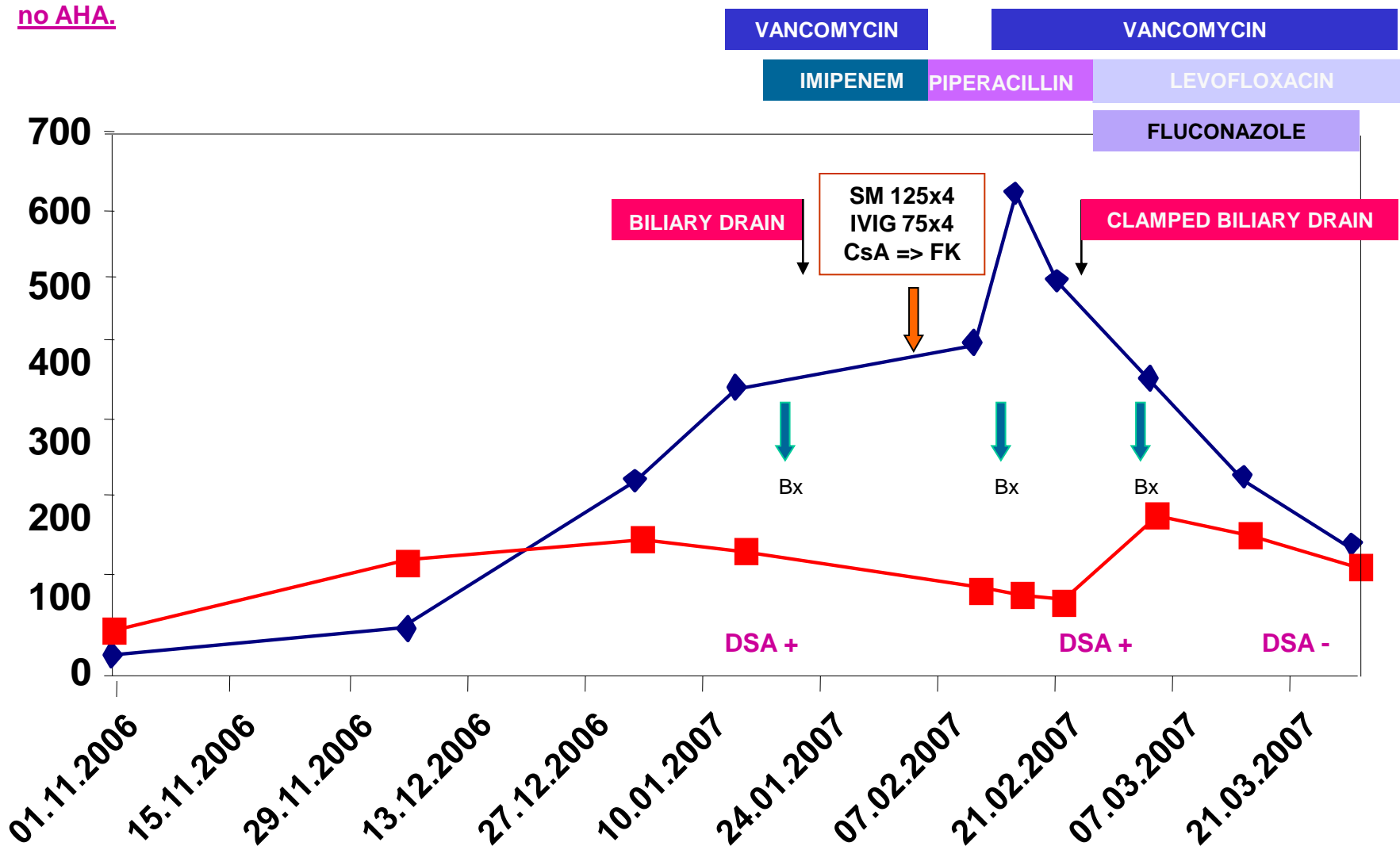
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M. G., 1946.  
OLT 26.09.2004  
14.06.04 and  
18.03.2005:  
no AHA.

◆ Bilirubin

■ ASAT



# RISCHI DELL'IMMUNOSOPPRESSIONE

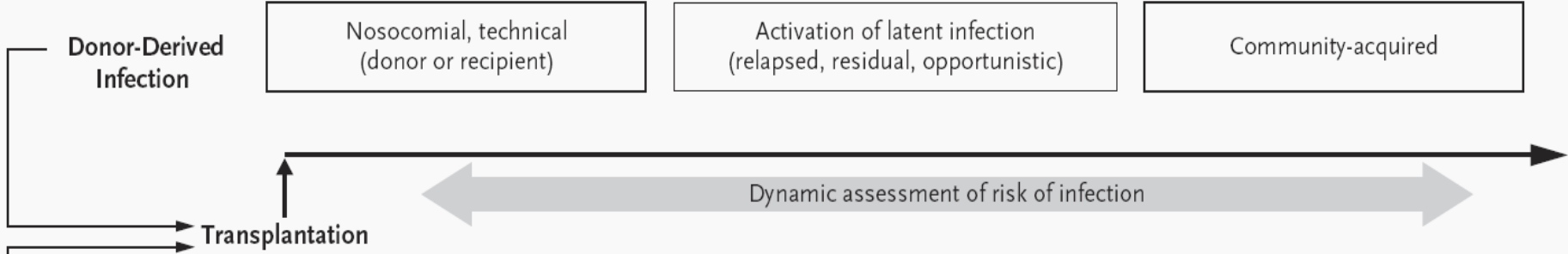
Infezioni virali (CMV, EBV, BKV, HHV6, HHV8, parvovirus B19, West Nile virus)  
batteriche, fungine.

Tumori (cute, linfomi).

Metabolismo: lipidi, diabete, ipertensione.

Nefrotossicità diretta Csa, FK.

# INFECTIONS *NEJM december 2007*



## Common Infections in Solid-Organ Transplant Recipients

	<1 Month	1–6 Months	>6 Months
<b>Donor-Derived Infection</b>			
<b>Recipient-Derived Infection</b>			
	<p>Infection with antimicrobial-resistant species:</p> <ul style="list-style-type: none"> <li>MRSA</li> <li>VRE</li> <li>Candida species (non-albicans)</li> </ul> <p>Aspiration</p> <p>Catheter infection</p> <p>Wound infection</p> <p>Anastomotic leaks and ischemia</p> <p><i>Clostridium difficile</i> colitis</p> <p>Donor-derived infection (uncommon):</p> <ul style="list-style-type: none"> <li>HSV, LCMV, rhabdovirus (rabies), West Nile virus, HIV, <i>Trypanosoma cruzi</i></li> </ul> <p>Recipient-derived infection (colonization):</p> <ul style="list-style-type: none"> <li>Aspergillus, pseudomonas</li> </ul>	<p>With PCP and antiviral (CMV, HBV) prophylaxis:</p> <ul style="list-style-type: none"> <li>Polyomavirus BK infection, nephropathy</li> <li><i>C. difficile</i> colitis</li> <li>HCV infection</li> <li>Adenovirus infection, influenza</li> <li><i>Cryptococcus neoformans</i> infection</li> <li><i>Mycobacterium tuberculosis</i> infection</li> </ul> <p>Anastomotic complications</p> <p>Without prophylaxis:</p> <ul style="list-style-type: none"> <li>Pneumocystis</li> <li>Infection with herpesviruses (HSV, VZV, CMV, EBV)</li> <li>HBV infection</li> <li>Infection with listeria, nocardia, toxoplasma, strongyloides, leishmania, <i>T. cruzi</i></li> </ul>	<p>Community-acquired pneumonia, urinary tract infection</p> <p>Infection with aspergillus, atypical molds, mucor species</p> <p>Infection with nocardia, rhodococcus species</p> <p>Late viral infections:</p> <ul style="list-style-type: none"> <li>CMV infection (colitis and retinitis)</li> <li>Hepatitis (HBV, HCV)</li> <li>HSV encephalitis</li> <li>Community-acquired (SARS, West Nile virus infection)</li> <li>JC polyomavirus infection (PML)</li> <li>Skin cancer, lymphoma (PTLD)</li> </ul>

Sig. E.S. – 10.04.1963



- Fasciite necrotizzante: *Staphylococcus aureus*
- Débridement chirurgico, ttt Augmentin
- Trapianto di pelle Thiersch

# TUMORI

- Cute  
(carcinomi spinocellulari,  
basocellulari)
- Malattie linfoproliferative  
(rare !)

# TUMORI CUTANEI

- Prevenzione:
  - Fotoprotezione
  - Minimizzare immunosoppressione

# METABOLISMO

- Lipidi
- Diabete
- Ipertensione

# IMMUNOSOPPRESSIONE E NEFROTOSSICITA

MINIMIZZARE I TASSI DI CNI (ciclosporina e tacrolimus)

CONTROLLARE :

- Dislipidemia
- Diabete
- Ipertensione arteriosa

NEFROPROTEZIONE :

- IECA (cave : creatinina, K<sup>+</sup>), per es. Zestril 2.5 mg
- Calcio-antagonisti (arteriola afferente)

# CAVE

- Preparati con *Saccharomyces boulardii* (Perenterol®)
- Klacid® e Diflucan®: aumento del T0  
CNI
- Pillola: Cérazette®
- Lipidi: Lescol® (+ Ezetrol®)

# DIMINUIZIONE INFIAMMAZIONE

- Può mascherare **addome acuto**:
  - Colecistite (salvo Tx fegato)
  - Diverticolite
  - Perforazione gastrointestinale
  - Colangite
  - ...

**ATTENZIONE**

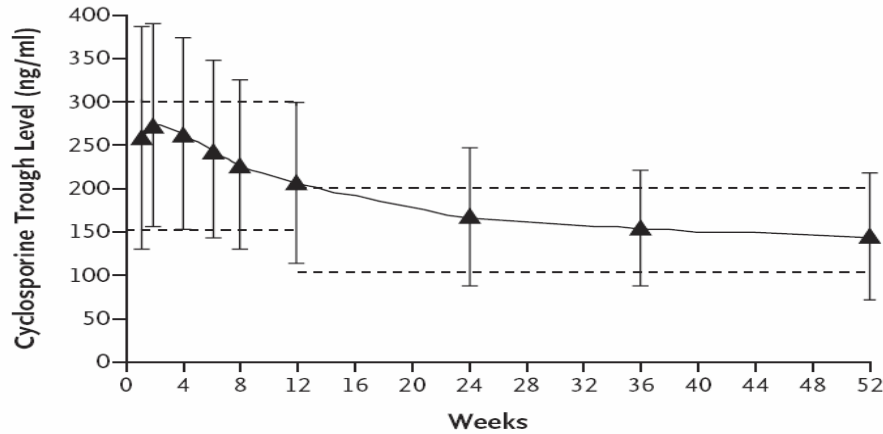
**RECIDIVA**

**DELLA**

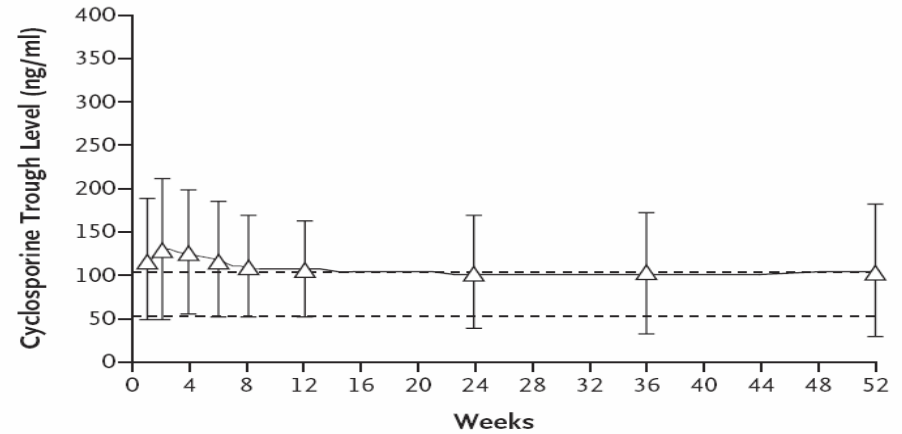
**MALATTIA DI BASE**

# SYMPHONY

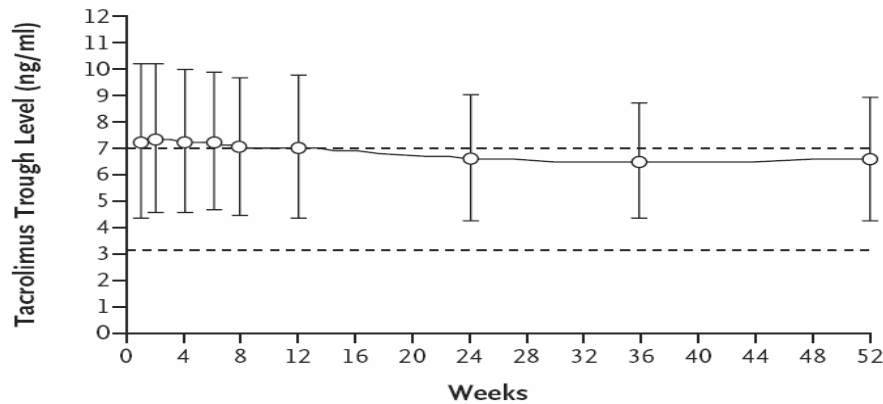
**A Standard-Dose Cyclosporine**



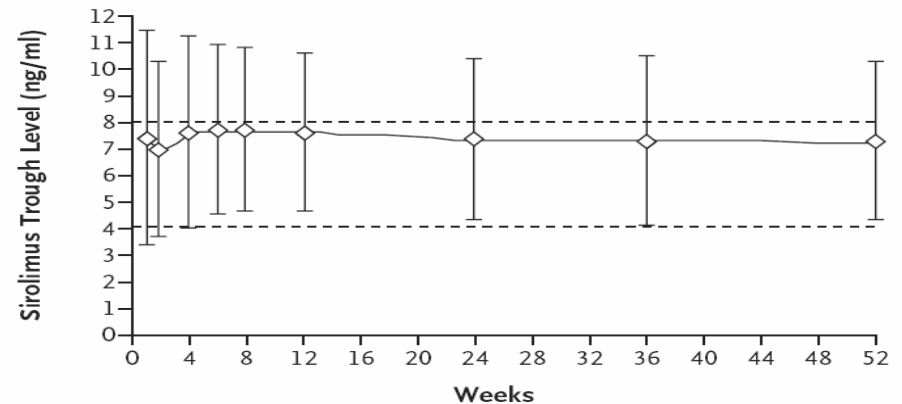
**B Low-Dose Cyclosporine**



**C Low-Dose Tacrolimus**



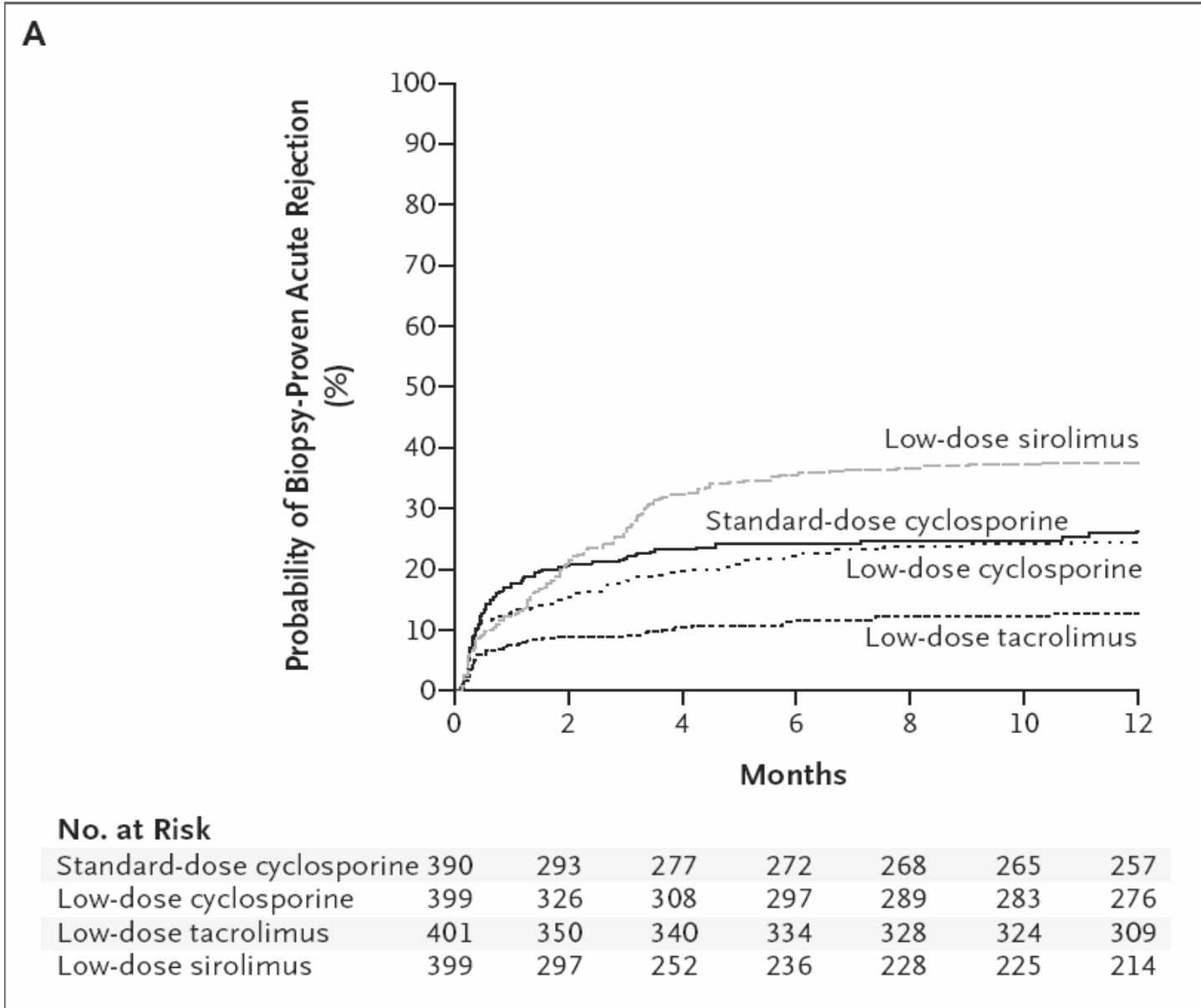
**D Low-Dose Sirolimus**



**Figure 2. Mean Trough Levels of Cyclosporine, Tacrolimus, and Sirolimus, According to Study Group.**

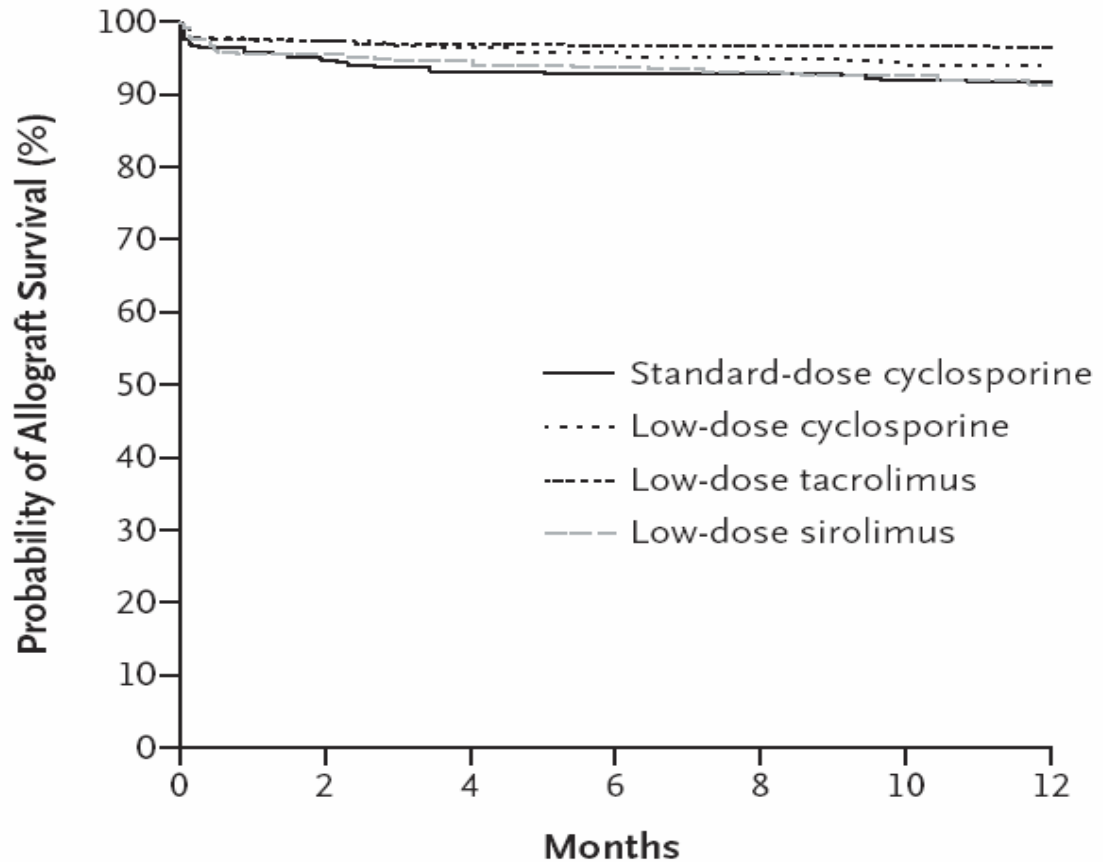
Kidney-transplant recipients in all four study groups were treated with mycophenolate mofetil and corticosteroids for 1 year in addition to the assigned study drug. Patients in the low-dose cyclosporine group, the tacrolimus group, and the sirolimus group also received daclizumab induction. Data are for the intention-to-treat population. Data are excluded for patients with standard-dose cyclosporine values of less than 49.0 ng per milliliter or more than 808.0 ng per milliliter, low-dose cyclosporine values of less than 29.0 ng per milliliter or more than 690.8 ng per milliliter, low-dose tacrolimus values of less than 2.2 ng per milliliter or more than 18.4 ng per milliliter, and low-dose sirolimus values of less than 2.2 ng per milliliter or more than 24.3 ng per milliliter. The dashed lines represent the upper and lower limits of the respective target trough levels. To convert the values for cyclosporine, tacrolimus, and sirolimus to nanomoles per liter, multiply by 0.83, 1.24, and 1.09, respectively. The I bars represent standard deviations.

# SYMPHONY (II)



# SYMPHONY (III)

**B**



**No. at Risk**

Standard-dose cyclosporine	390	359	345	341	338	333	325
Low-dose cyclosporine	399	381	371	367	363	355	345
Low-dose tacrolimus	401	381	374	371	367	363	349
Low-dose sirolimus	399	373	364	358	349	344	329

# REGISTRO OPELZ

- Attenzione comunque alla diminuzione, anche se tardiva, dell'immunosoppressione

# ASPETTI PSICOLOGICI

- Vissuto pre-Tx
- Vissuto post-Tx
- Identità del donatore (e/o famiglia)

Grazie per la vostra attenzione

