

IX Corso di Aggiornamento sul  
Trapianto di Rene

2011 Pavia



Plasmapheresis and Immunoabsorption  
for sensitized patients  
awaiting cadaveric kidney transplantation



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# Why we need Desensitization...

## Kidney Graft Survival Rates

<b>PRA</b>	<b>Post TX (years)</b>	<b>% Graft survival</b>
0-9%	5	72
10-79%	5	66
80+%	5	62

## Kidney Median Waiting Times

<b>PRA</b>	<b>Time (days)</b>
0-9%	1329
10-79%	1920
80+%	3649

**UNOS**

Based on OPTN data as of July 1, 2011

# Principles of Desensitization

## Antibody Removal

Plasmapheresis

Immunoadsorption

## Immunomodulation

IVIg

ATG

Rituximab

Bortezomib

reduce broadness → increase chance for XM neg. offer  
reduce strength → reduce TX rejection  
overcome pos XM → enable TX

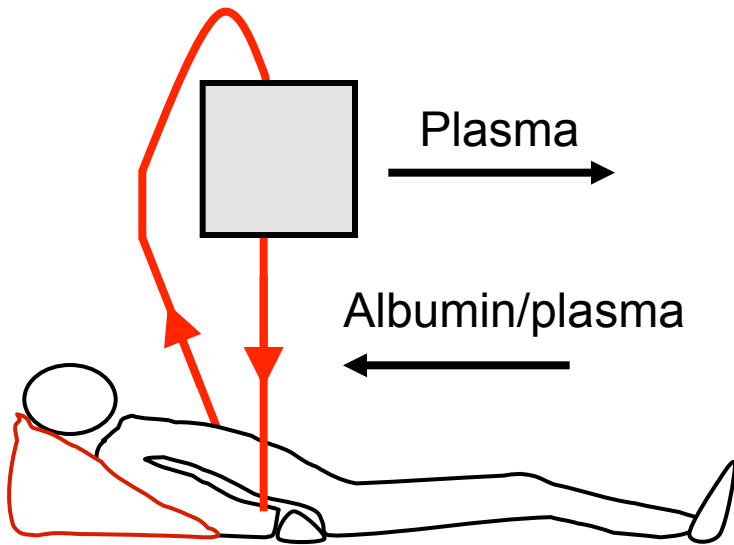
# Major Indications & Protocols

<b><i>INDICATIONS</i></b>	<b><i>PROTOCOLS</i></b>		
	<b>PP/IVIG<sub>low</sub></b>	<b>IA</b>	<b>IVIG<sub>high</sub></b>
<b>XM Conversion (LD)</b>	yes	yes	yes*
<b>Desensitization (wait list, DD)</b>	yes	yes	yes*
<b>Rapid Desensitization (after TX offer, DD)</b>	yes	yes	no

\*randomized controlled trial (NIH)

# Principles of Apheresis

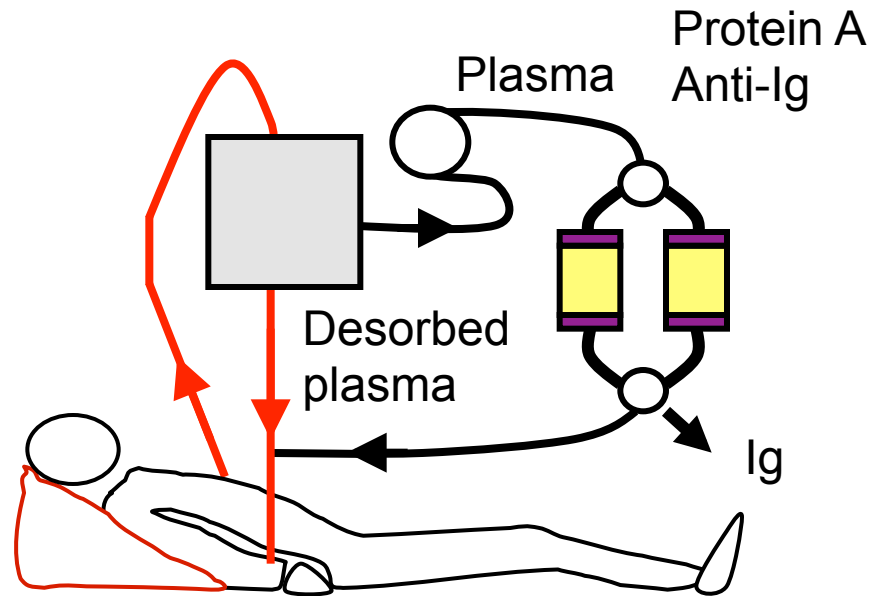
## Plasmapheresis



Non-selective depletion  
of plasma proteins

Cave: Coagulation factors

## Immunoabsorption



Selective antibody  
depletion

# 1. Desensitization on the Wait List (DD)

Author, yr	N	Apheresis	IVIg <i>low</i>	TX	Waiting Time (m)	Outcome
Taube, 1984						
Palmer, 1989						
Kupin, 1991	Hi					
Hiesse, 1992	Gi			worse than	IS w/o TX	Guaranty
Ross, 1993	nc			patients		
Reisaeter, 1995	Nc			low up		
Yuan, 2010						

# Desensitization on the Wait List: Norway

**78 patients**

**Death 3 patients due to sepsis during PP  
9 non transplanted → 66 DD TX**

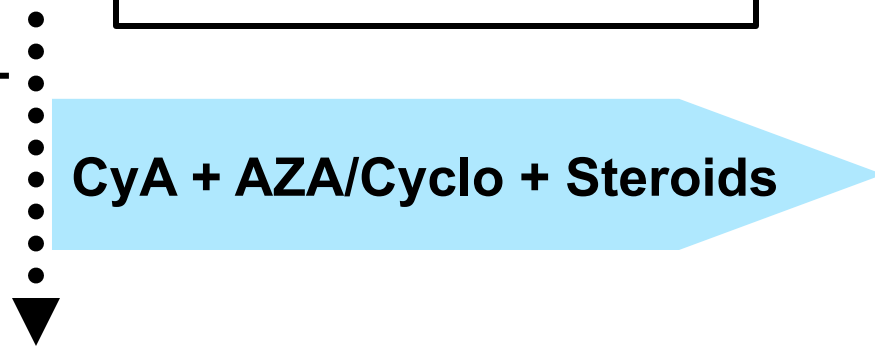
**Risk - Benefit?  
stay on dialysis...**

**AR < 3month post TX 89%**  
  
**1 graft survival**  
1<sup>st</sup> TX (n = 27): 70%  
Re TX (n = 39): 61%  
  
**4 graft survival**  
1<sup>st</sup> TX: 57%  
Re TX: 47%

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**Withdrawal after 6 month**

**PRA reduction only in 60% !**



Live-donor transplantation after desensitization provided a **survival benefit**, as compared with waiting for a compatible organ.

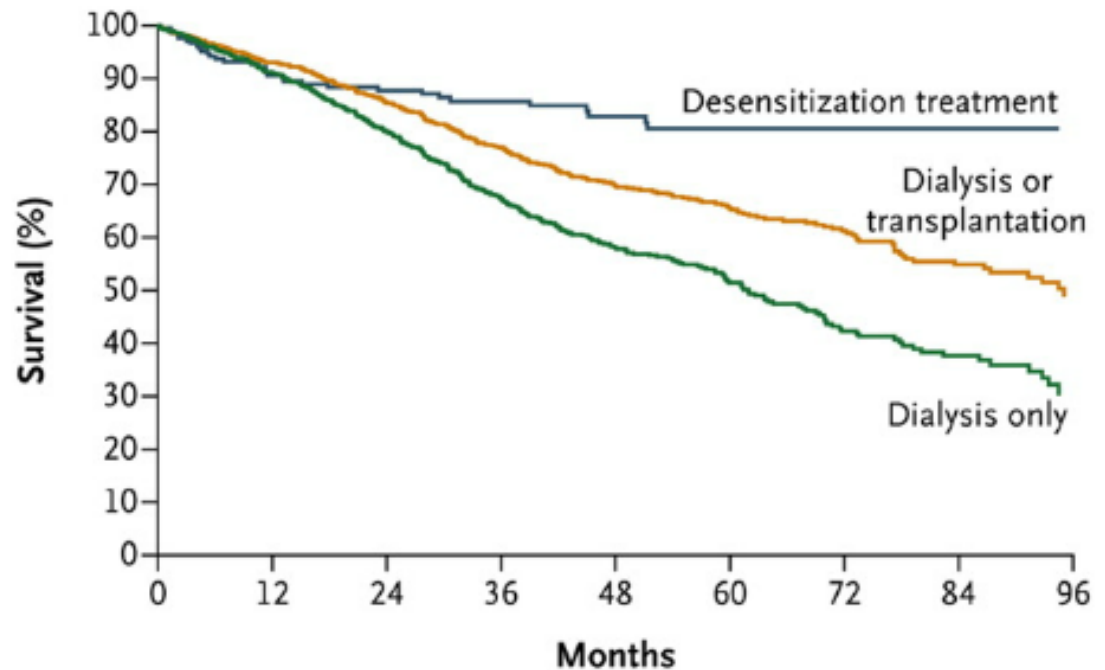
NIH sponsored

Case control

211 LDs: PP+IVIG<sub>low</sub>

> 1000 controls

Long term follow up survival data



## 2. Rapid Desensitization (DD): 1-shot / peri-TX

Author, yr	N	Apheresis	Additional Induction	1-shot/ peri-TX	Outcome
Paln					71% AR, 30% GS
Higg					14% GS
Lore					75% GS at TX
Mag					39% GS
Bein					00% GS
Bartel, 2010	68	IA	ATG	peri-TX	30% AR, 70% GS 7a post TX

**Ratio: prevent AB rebound  
seen on waiting list protocols**

**Problem: short window for treatment  
before TX**

# “One shot” pre-TX Immunoabsorption

## Patient Characteristics N=13

CDC-PRA 18 – 100%  
CDCXM+ N=9

until XM Conversion !  
up to 22h

IA

TX



## 2a Follow-up

Acute rejection 9/13

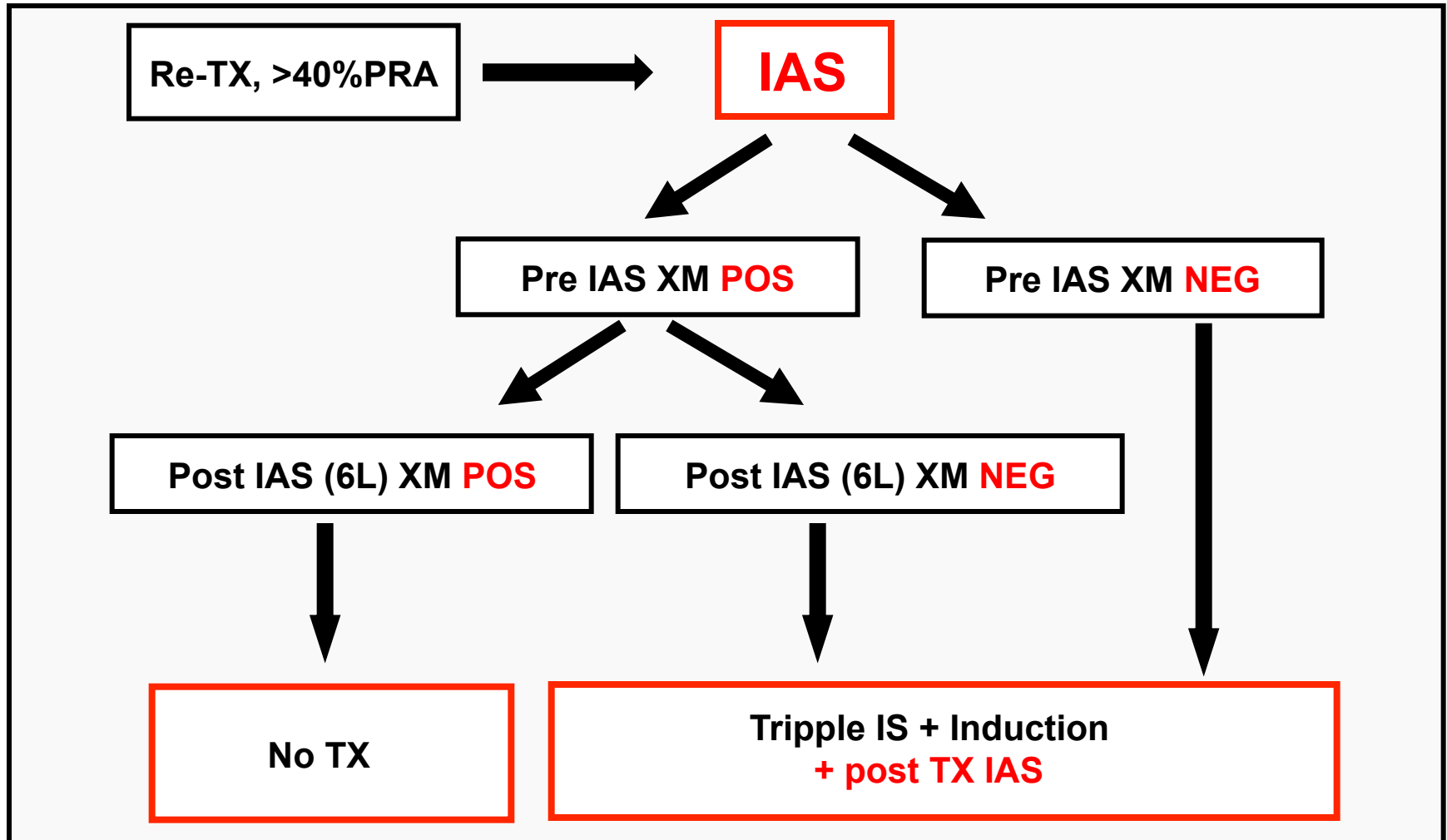
Graft Loss 6/13

Creatinine (mg/dl) 2.5

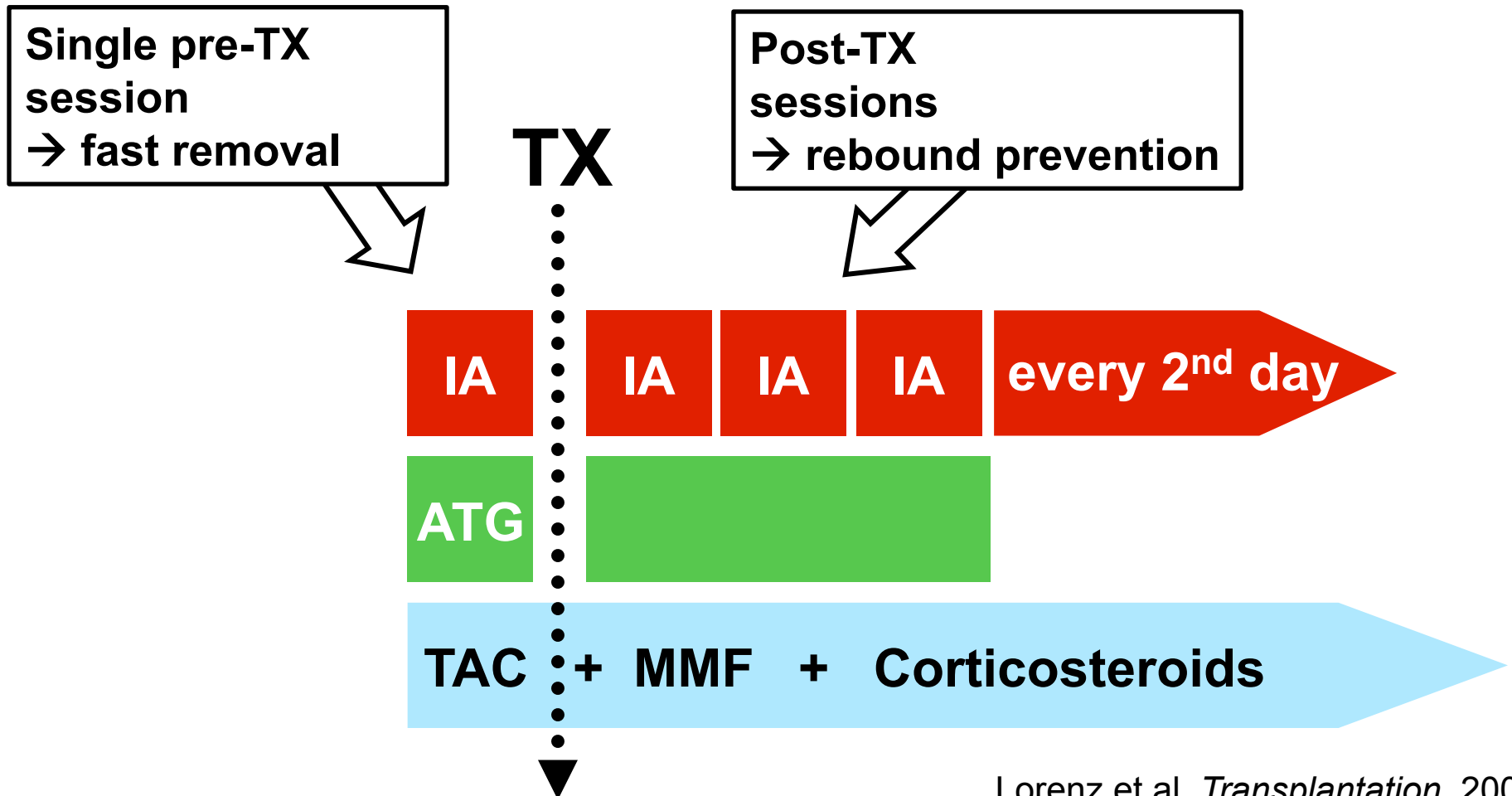
Cold Ischaemia Time 28–62 h

**How can we beat CIT  
and post NTX AB rebound?**

# Peri-TX apheresis (Vienna protocol)



# Peri-TX apheresis for DD: Vienna protocol

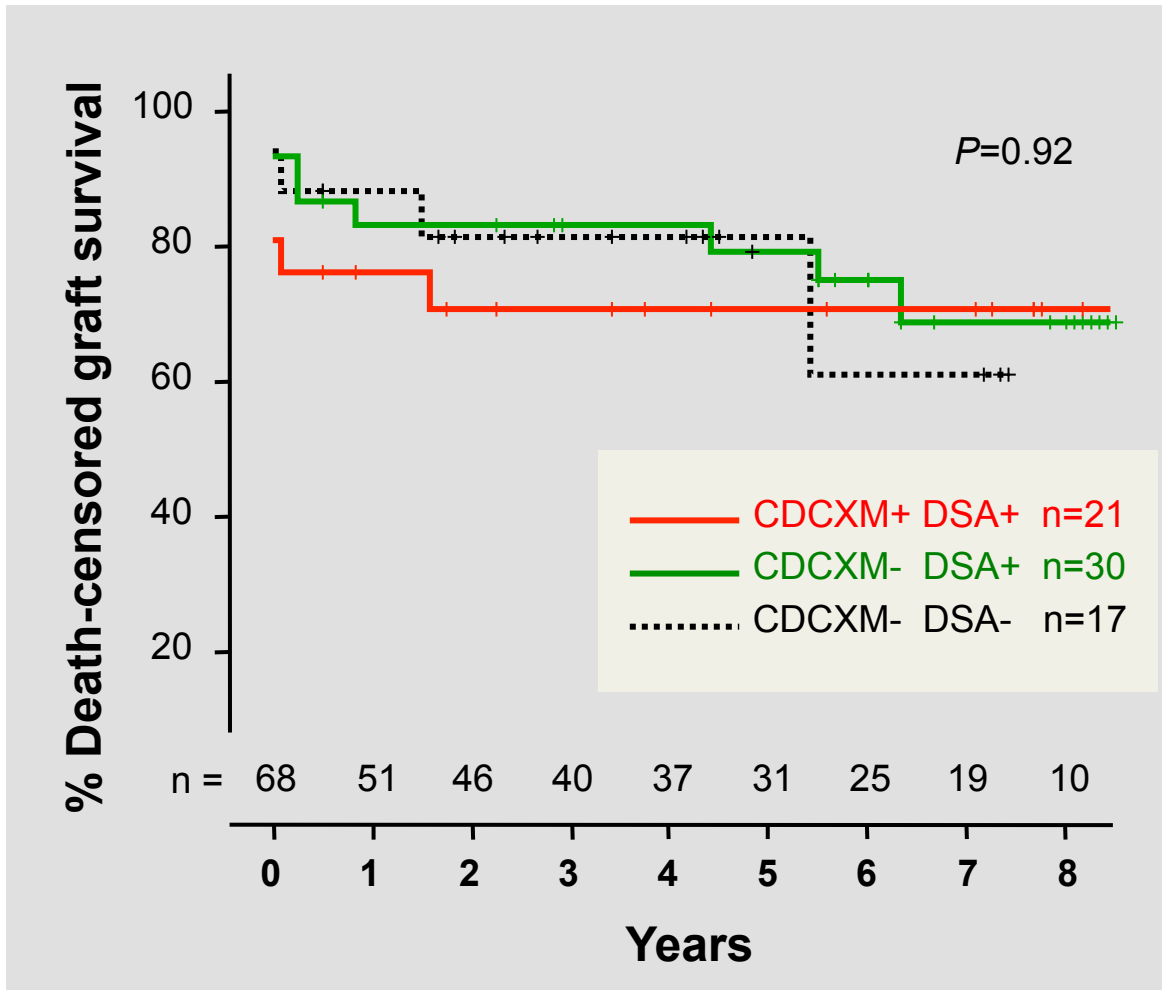


**68 DD Patients**

65 Re-TX

CDC-PRA 73%

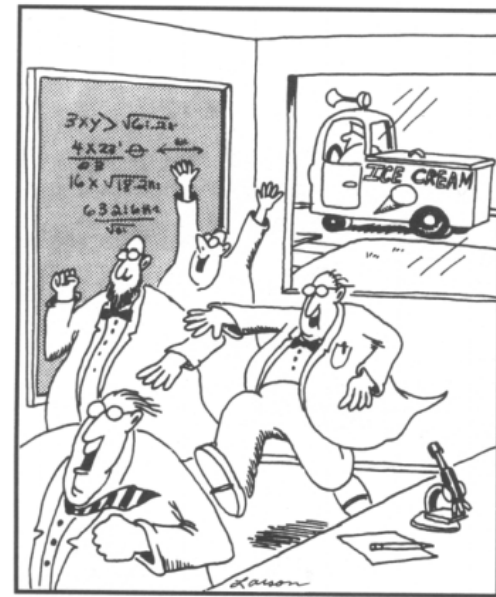
51 DSA + / 21 CDCXM +



	<b>CDCXM + (N=21)</b>	<b>CDCXM-/DSA+ (N=30)</b>	<b>CDCXM-/DSA- (N=17)</b>	<b>P value</b>
<b>Acute cellular rejection</b>	14%	24%	18%	0.7
Banff I, N	0	3	0	
Banff II, N	3	4	3	
<b>Acute (C4d+) AMR</b>	<b>19%</b>	<b>23%</b>	<b>24%</b>	<b>0.92</b>
Banff I	1	3	2	
Banff II	3	4	2	
<b>Chronic (C4d+) AMR</b>	<b>5%</b>	<b>10%</b>	<b>6%</b>	<b>0.75</b>
<b>Delayed graft function, N (%)</b>	38%	47%	47%	0.74
<b>Median 3-yr SrCr (mg/dL)</b>	1.3	1.6	1.5	0.78
<b>Median 3-yr Protein excr. (g/L)</b>	<0.05	<0.05	<0.05	0.18

# Take Home Message

What can **Apheresis** offer the highly **sensitized patient** waiting for **cadaveric NTX**...



**Desensitization** on the waiting list

- Reduced waiting times BUT
- Short term outcome not satisfying, long term outcome?  
high AR, unnecessary IS

*Evidence Level B (no RCT)*

**Rapid Desensitization** after TX offer

1. One shot, 2. peri-TX Apheresis
- Reduced waiting times, acceptable long term graft survival and AR rates

*Evidence Level B (no RCT)*



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Heinz Regele

**Department of Blood Group Serology**

Gottfried Fischer

Bettina Haidbauer

**Department of Surgery**

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**Detailed immunological evaluation**  
Complementary use of cell-based and solid phase assays

**Live Donor**

**Deceased Donor**

**Kidney Paired Donation**  
Altruistic Donors,  
Live donor kidney transport  
*Evidence B*

**Specific Allocation**  
Calculated PRA,  
Acceptable Mismatch Program  
*Evidence B*

and

**Desensitization on the waiting list**  
IVIg based *Evidence A*  
PP based *Evidence B*

and/or

**Desensitization**  
IVIg based  
*Evidence B*  
PP based  
*Evidence B*

**Rapid XM Conversion**  
Peri-TX IA  
*Evidence B*