



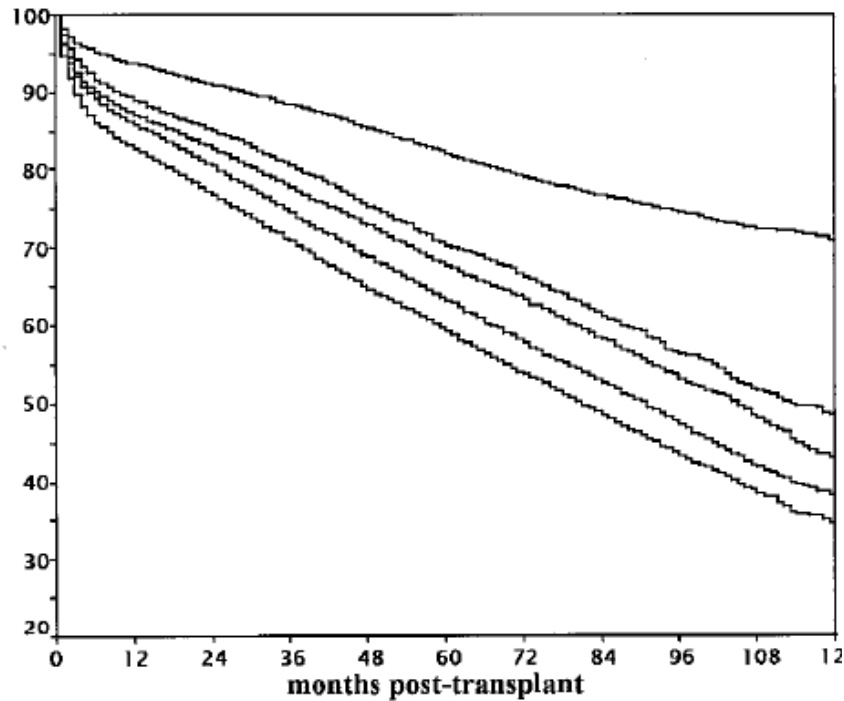
Trapianto Renale in Incompatibilita' ABO

Lucrezia Furian

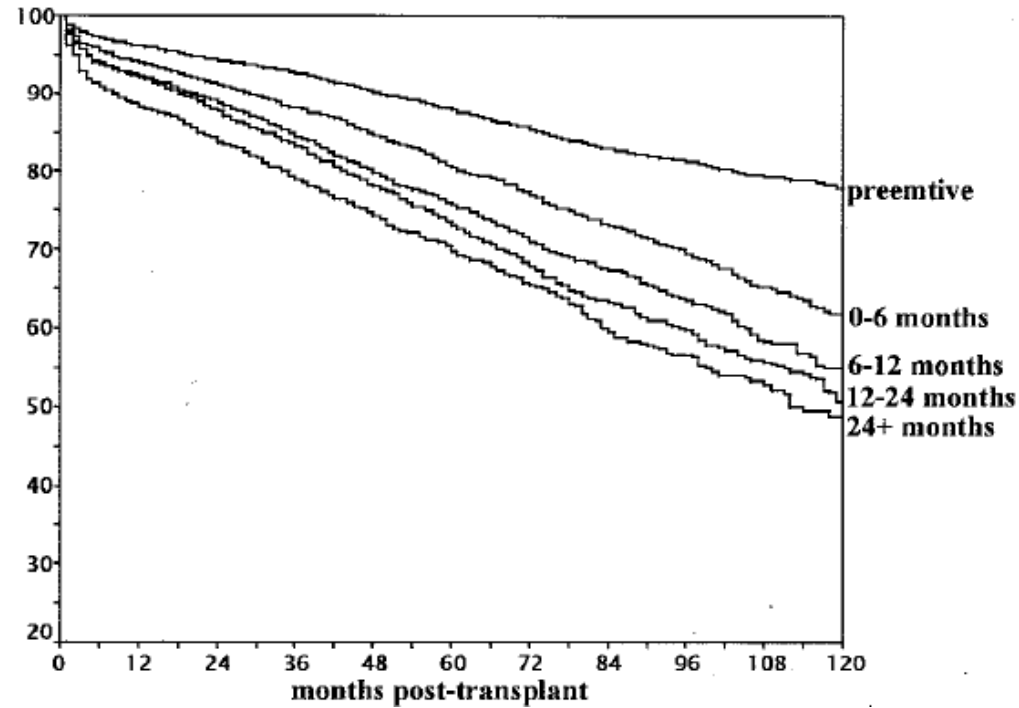
**U.O.C. Trapianti Rene e Pancreas
Direttore: Prof. Paolo Rigotti
Azienda Ospedale Università di Padova**

Graft survival Deceased vs Living Donor

Deceased donors



Living donors



O_{ag}

anti A Ab
anti B Ab

45%

A_{ag}

(A₁ ~36%, A₂ ~9%)

anti B Ab

10%

B_{ag}

anti A ab

La probabilità che due
individui siano AB0
incompatibili è del

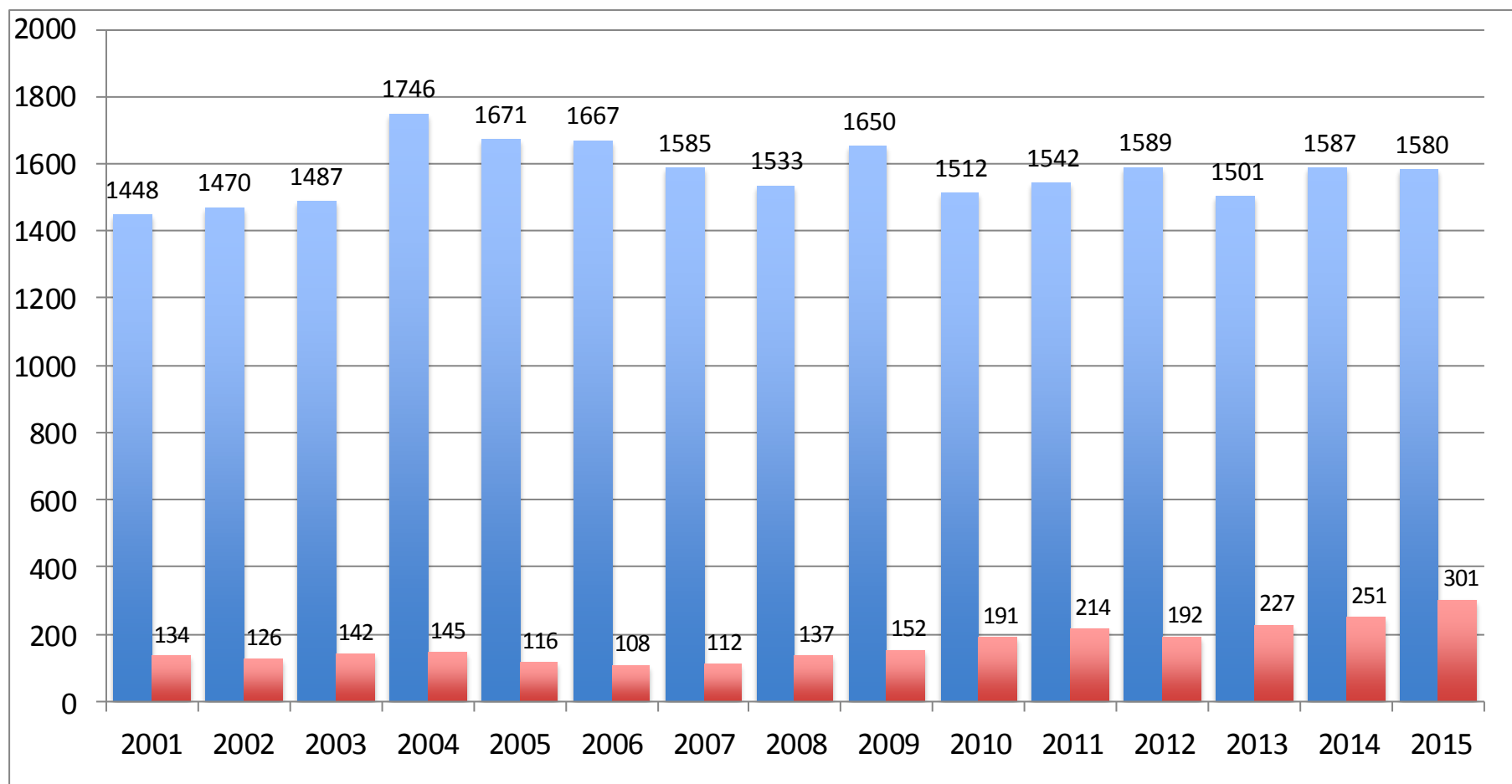
35,75%

A_{ag}B_{ag}

no Ab

5%

Trapianti di rene da donatore vivente in Italia 2001-2015



Centro Nazionale Trapianti



Trapianti di rene da donatore deceduto



Trapianti di rene da donatore vivente

Fonte SIT: Sistema informativo trapianti



Rete
Nazionale
Trapianti

Trapianto di rene ABO incompatibile

MILESTONES



First ABOi tx in Japan:

- Splenectomy
- Plasmapheresis
- Azathioprine
- Cyclosporine
- Steroids



Immunoadsorption

Basiliximab

1987

1989

2001

2002

2004

2005

1982-1987

ABOi tx in Belgium:

- Platelets donor transfusion
- Plasmapheresis
- Splenectomy
- Cyclosporine
- Azathioprine
- Polyclonal Ab

MMF replaced Azathioprine

RITUXIMAB replaced splenectomy



Il trapianto di rene ABO incompatibile: l'esperienza internazionale



Excellent Long-term Outcome of ABO-Incompatible Living Donor Kidney Transplantation in Japan

Takahashia K et al., AJT:2004; 4: 1089–1096



Plasmapheresis, CMV Hyperimmune Globulin, and Anti-CD20 Allow ABO-Incompatible Renal Transplantation Without Splenectomy

Christopher J. Sonnenday C.J. et al., AJT: 2004; 4: 1315–1322



ABO Incompatible Kidney Transplantations Without Splenectomy, Using Antigen-Specific Immunoabsorption and Rituximab

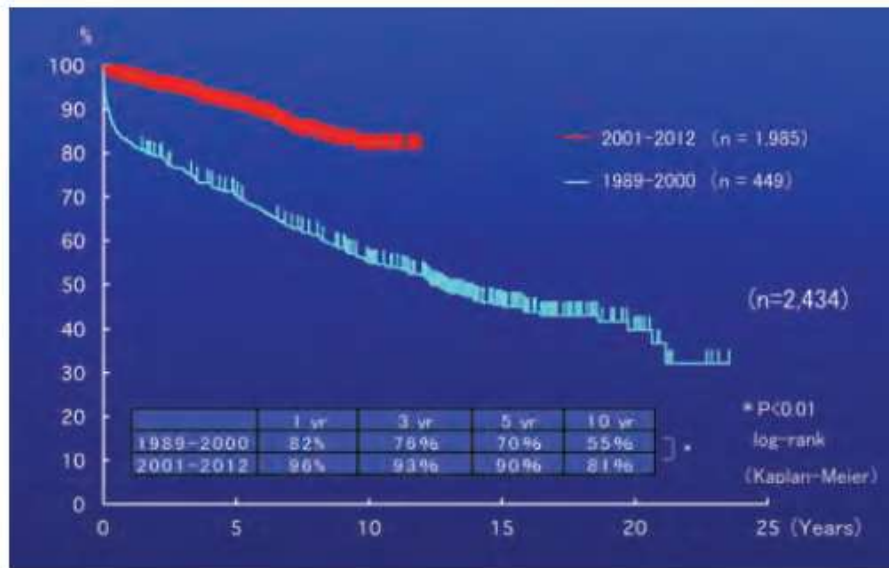
Tyden G et al., AJT: 2005; 5: 145–148



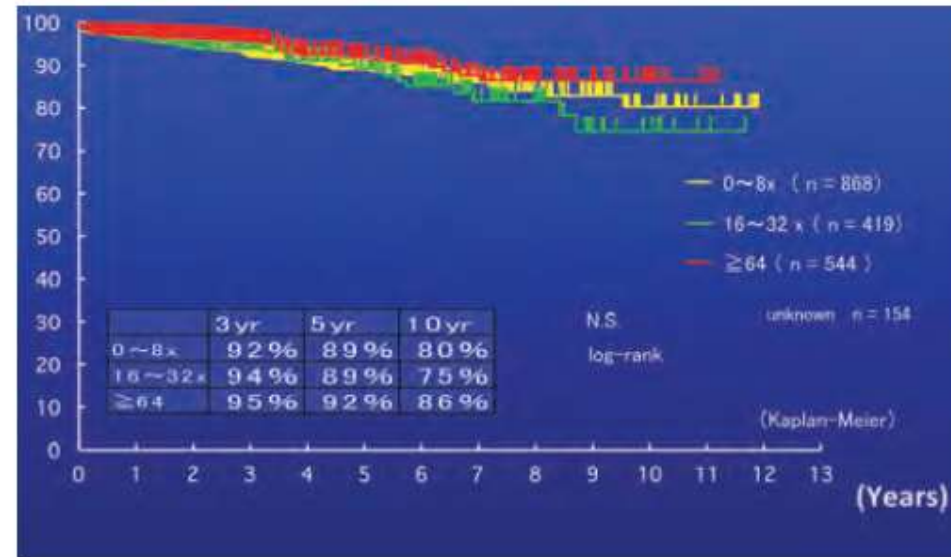
ABO Incompatible Kidney Transplant: LONG TERMS RESULTS

Trends in ABO-Incompatible Kidney Transplantation

Aikawa A. et al.; Exp Clin Transplant 2015 Suppl 1: 18-22



Graft Survival 1989-2000 compared with 2001-2012



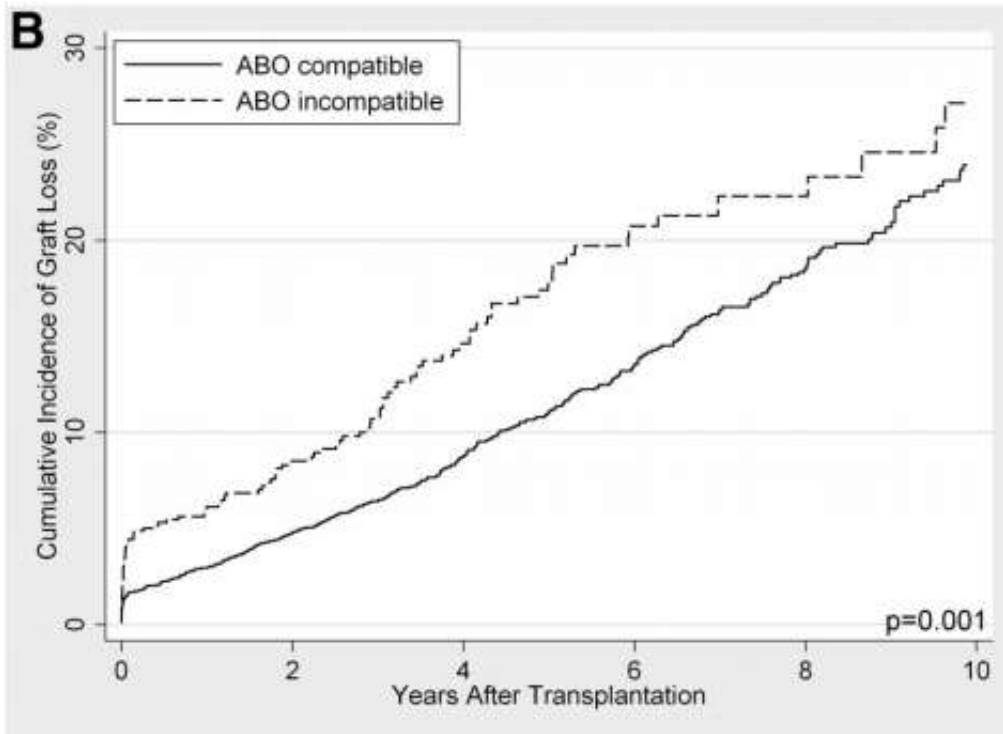
Graft Survival according to IgG titer (2001-2012)



ABO Incompatible Kidney Transplant: LONG TERMS RESULTS

Outcomes of ABO-Incompatible Kidney Transplantation in the United States

John R. Montgomery,¹ Jonathan C. Berger,¹ Daniel S. Warren,¹ Nathan T. James,¹ Robert A. Montgomery,¹
and Dorry L. Segev^{1,2,3}



**738 ABOi KT
from 280 Transplant Centres
Graft survival:**

94.1% ➡ **1 year**

89.6% ➡ **3 years**

82.6% ➡ **5 years**

72.9% ➡ **10 years**



ABO Incompatible Kidney Transplant: LONG TERMS RESULTS

Implementation of a Protocol for ABO-Incompatible Kidney Transplantation – A Three-Center Experience With 60 Consecutive Transplantations

Gunnar Tydén,^{1,4} Johannes Donauer,² Jonas Wadström,³ Gunilla Kumlien,¹ Jochen Wilpert,²
Thomas Nilsson,³ Helena Genberg,¹ Przemislaw Pisarski,² and Gunnar Tufveson³

Transplantation 2007;83:1153

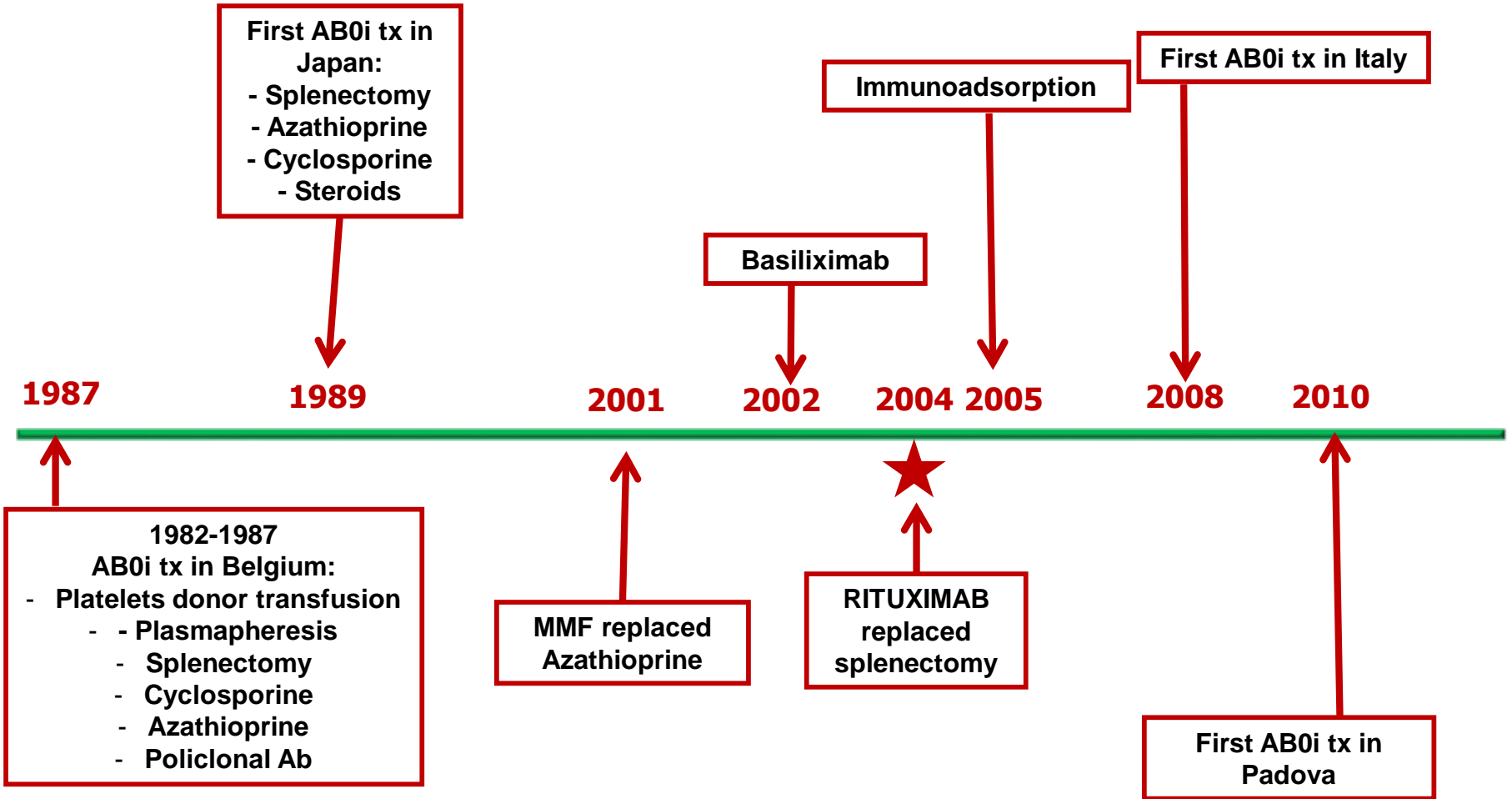
TABLE 1. Comparison of graft and patient survival and graft function in ABO-incompatible and ABO-compatible living-donor (LD) transplantations

	N	Graft losses	Actual graft survival	Actual patient survival	Actual serum creatinine ($\mu\text{mol/L}$) mean and range	Follow-up mean and range
<u>ABO-incompatible LD tx</u>	60	1 non-compliance 1 DWFG	97%	98%	127 (42–203)	17.5 (2–61) months
ABO-compatible LD tx	274	7 AHR+2 technical 6 DWFG	95%	98%	133 (53–360)	21.1 (2–63) months

AHR, acute humoral rejection; DWFG, death with functioning graft.

Trapianto di rene ABO incompatibile

MILESTONES





ABO incompatible Kidney transplant: The italian experience



PARMA: Rituximab+Immunoadsorption+IVIg

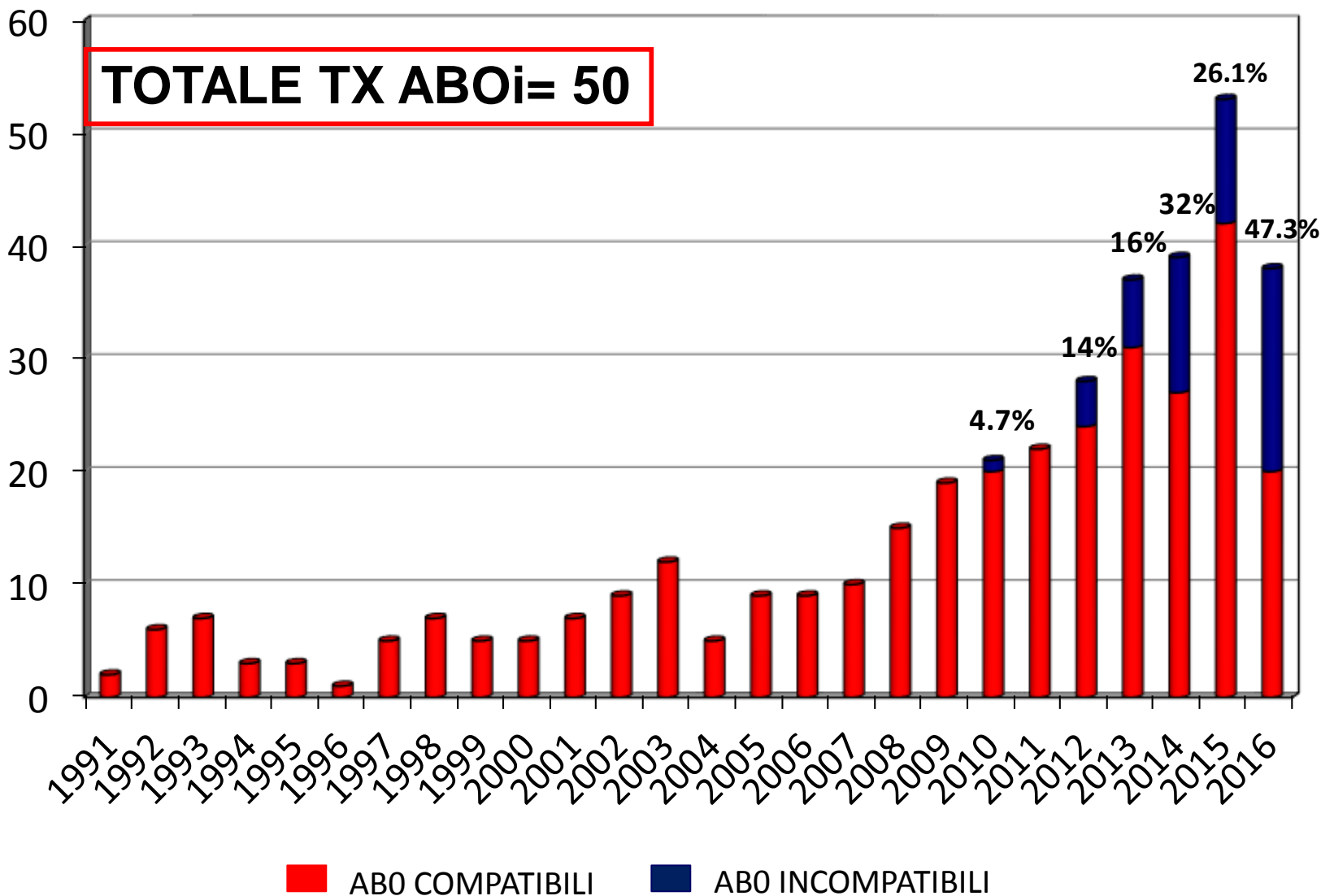
PADOVA: Rituximab+Plasmapheresis+CMV-IgG

PISA: Rituximab+Plasmapheresis+IVIg

**Kidney and Pancreas Transplantation Unit
University of Padua
July 2010 – November 2016
50 ABOi Living Donor
Transplants**

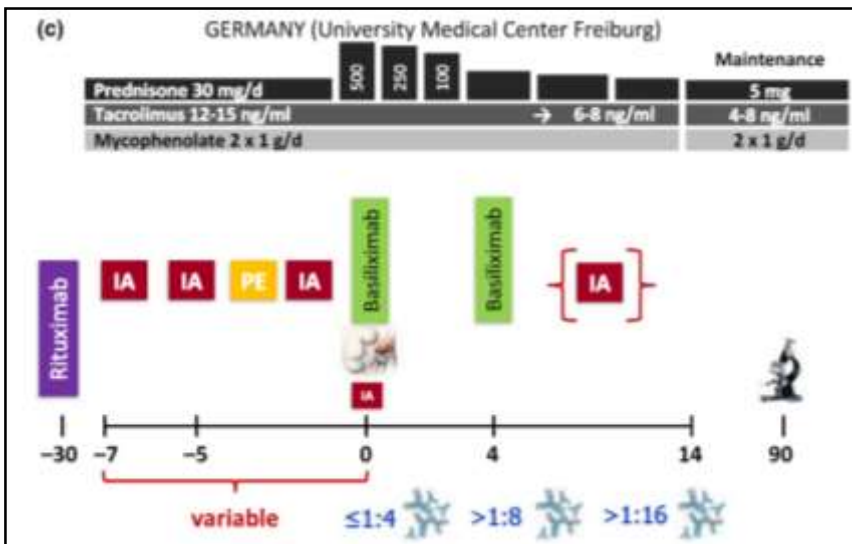
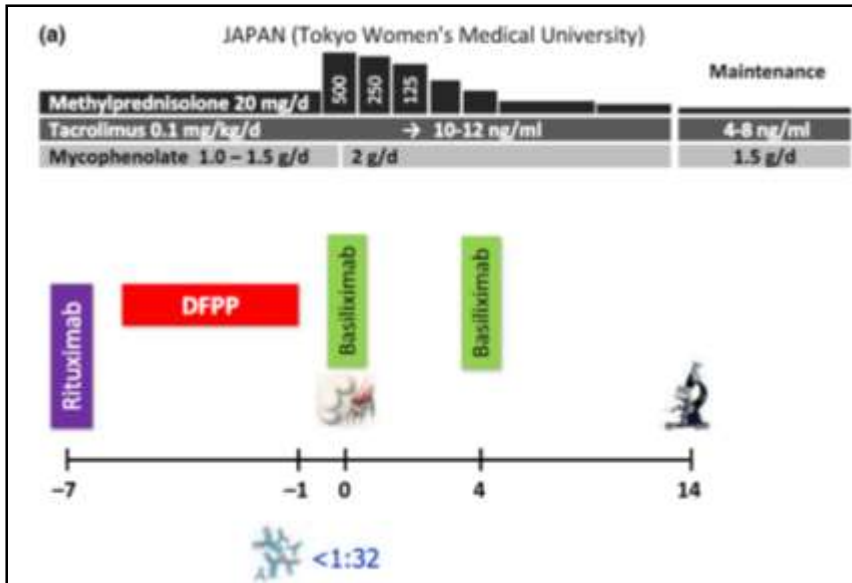
U.O.C. TRAPIANTI RENE E PANCREAS

TRAPIANTO DI RENE ABO INCOMPATIBILE: LA NOSTRA ESPERIENZA



An update on ABO-incompatible kidney transplantation

Stefan Zschiedrich,¹ Albrecht Kramer-Zucker,¹ Bernd Jänigen,² Maximilian Seidl,^{3,4} Florian Emmerich,⁵ Przemyslaw Pisarski² and Tobias B. Huber^{1,6,7}



Differences between these protocols include:

- ✓ timing and dosage of rituximab
- ✓ induction therapies and continuous immunosuppression
- ✓ isohaemagglutinin reduction techniques
- ✓ surveillance kidney graft biopsy



ABO Incompatible Renal Transplantation: A Paradigm Ready for Broad Implementation

Robert A. Montgomery,^{1,6} Jayme E. Locke,¹ Karen E. King,² Dorry L. Segev,¹ Daniel S. Warren,¹ Edward S. Kraus,³ Matthew Cooper,⁴ Christopher E. Simpkins,¹ Andrew L. Singer,¹ Zoe A. Stewart,¹ J. Keith Melancon,¹ Lloyd Ratner,⁵ Andrea A. Zachary,³ and Mark Haas²

TABLE 4. Patient and graft survival among 60 ABOi kidney transplant recipients transplanted at the Johns Hopkins Hospital between 1999 and 2007

Years posttransplant	ABOi cohort	
	Graft survival ^a (%)	Patient survival ^b (%)
1 yr	98.3	96.3
3 yr	92.9	96.3
5 yr	88.7	89.4

First Era—Splenectomy or Anti-CD20 or Both

Second Era—No Splenectomy and No Anti-CD20

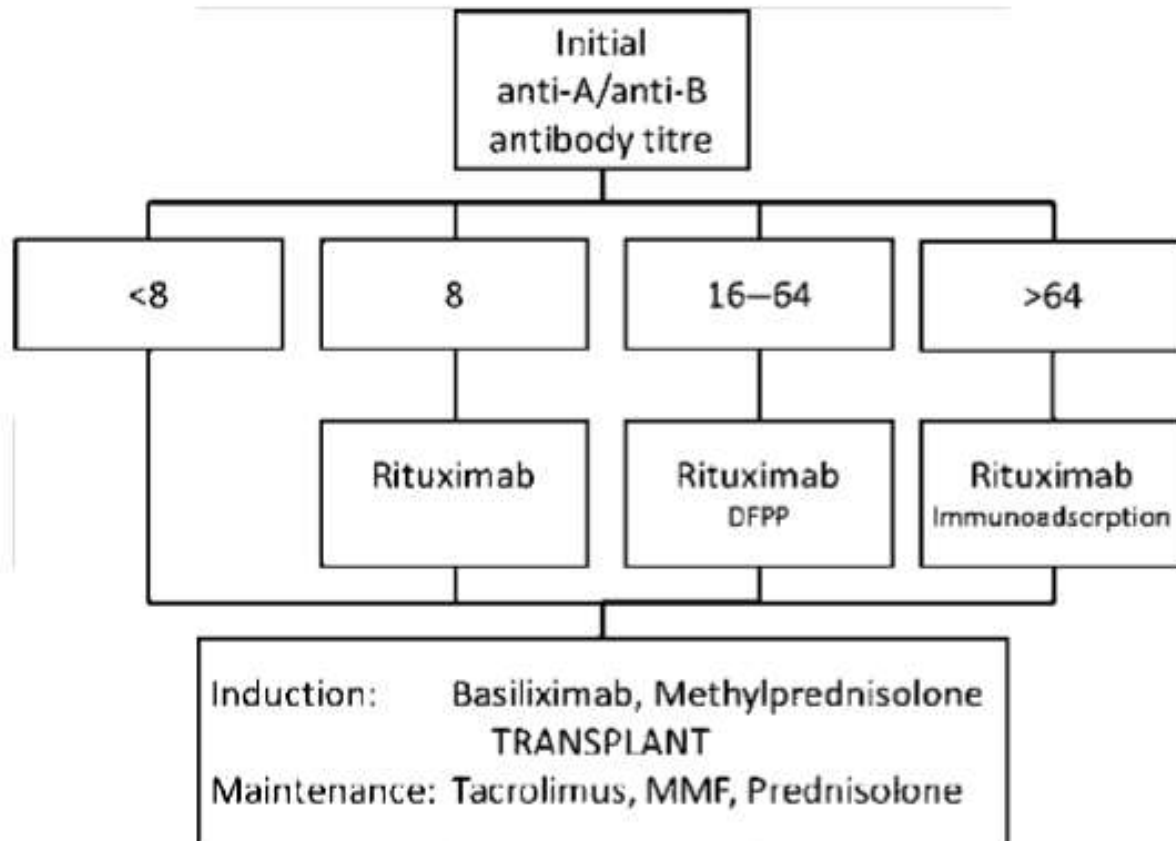
TABLE 6. Incidences of acute rejection episodes among ABO incompatible kidney transplant recipients transplanted at Johns Hopkins Hospital between 1999 and 2007

Rejection episodes	Overall	First era				28 PTS Second era ^b	HLA Identical/ ABOi	+XM/ABOi ^c
		14 PTS Splenectomy only	15 PTS Rituximab only	Splenectomy and rituximab	All treatments ^a			
Hyperacute	None	None	None	None	None	None	None	None
Clinical acute								
Antibody mediated	11	3	3	0	6	5	2	4
Cellular	11	0	6	2	8	3	1	3

Tailored desensitization strategies in ABO blood group antibody incompatible renal transplantation

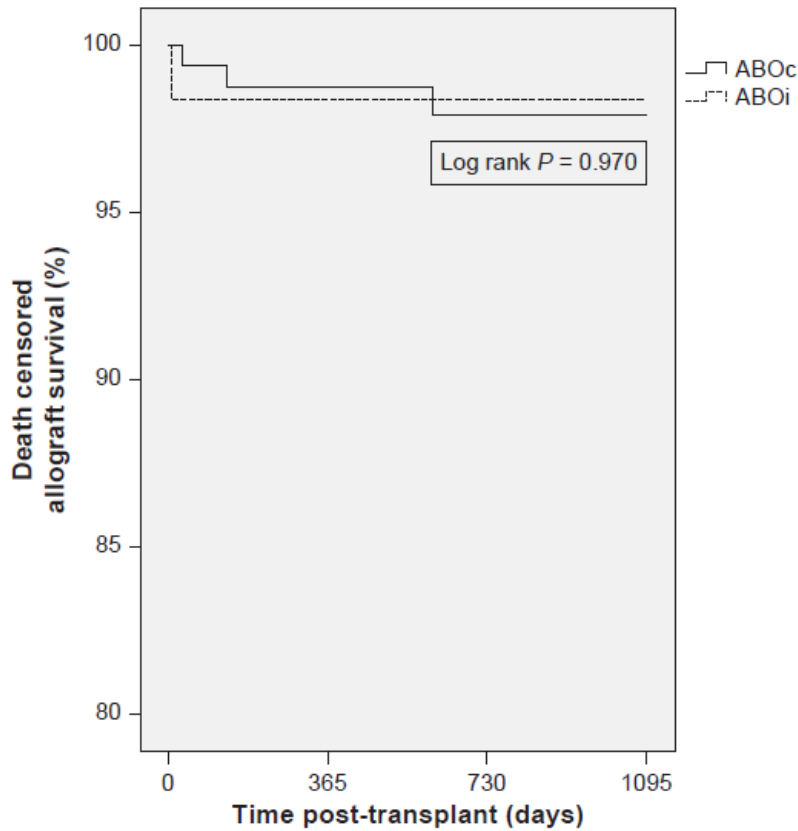
A. Nicholas R. Barnett,^{1,2} Miriam Manook,^{1,2} Myura Nagendran,¹ Shivakumar Kenchayikoppad,¹ Robert Vaughan,^{1,2,3} Anthony Dorling,^{1,2} Vassilis G. Hadjianastassiou^{1,2,4} and Nizam Mamode^{1,2}

Guy's Hospital minimal desensitization strategy

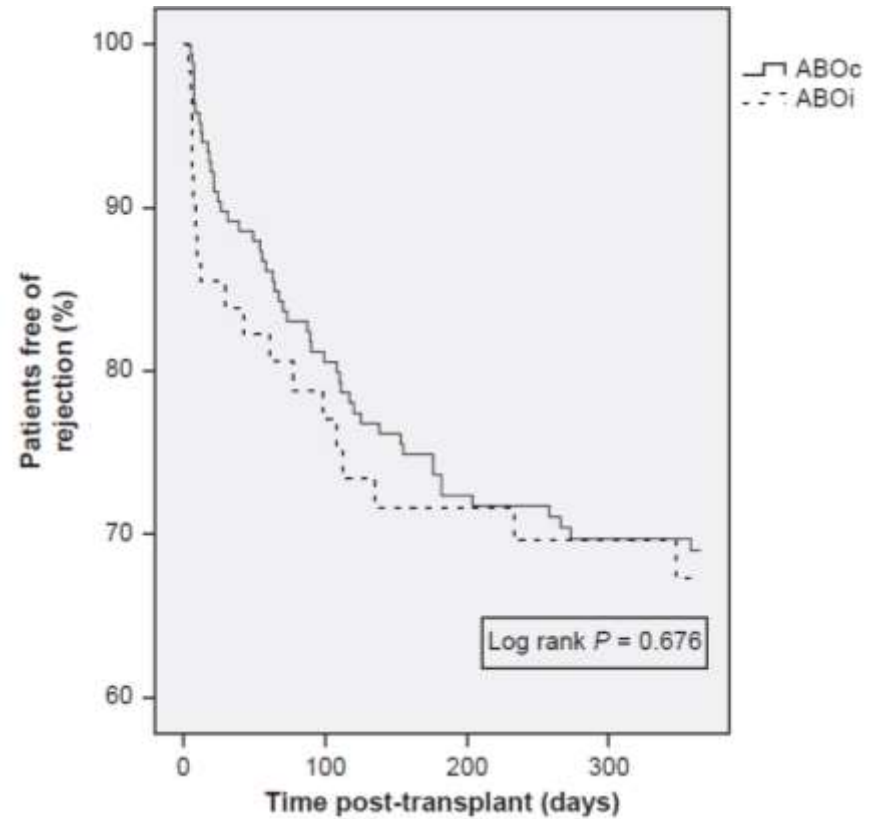


Tailored desensitization strategies in ABO blood group antibody incompatible renal transplantation

A. Nicholas R. Barnett,^{1,2} Miriam Manook,^{1,2} Myura Nagendran,¹ Shivakumar Kenchayikoppad,¹ Robert Vaughan,^{1,2,3} Anthony Dorling,^{1,2} Vassilis G. Hadjianastassiou^{1,2,4} and Nizam Mamode^{1,2}



Kaplan–Meier survival curve of death-censored allograft survival at 3 years post-transplant.



Kaplan–Meier survival curve of rejection-free survival 1 year post-transplant.

Tailored desensitization strategies in ABO blood group antibody incompatible renal transplantation

A. Nicholas R. Barnett,^{1,2} Miriam Manook,^{1,2} Myura Nagendran,¹ Shivakumar Kenchayikoppad,¹ Robert Vaughan,^{1,2,3} Anthony Dorling,^{1,2} Vassilis G. Hadjianastassiou^{1,2,4} and Nizam Mamode^{1,2}

	ABOi (<i>n</i> = 62)	ABOc (<i>n</i> = 167)	<i>P</i> -value*
1 year creatinine	151.45 (SD 80.19) <i>n</i> = 42	133.34 (SD 47.51) <i>n</i> = 134	0.368
2 year creatinine	139.44 (SD 59.49) <i>n</i> = 32	137.21 (SD 42.62) <i>n</i> = 101	0.854
3 year creatinine	131.82 (SD 34.11) <i>n</i> = 17	136.76 (SD 53.95) <i>n</i> = 75	0.888
1 year eGFR	47.15 (SD 20.16) <i>n</i> = 40	50.68 (SD 15.35) <i>n</i> = 134	0.188
2 year eGFR	46.50 (SD 15.19) <i>n</i> = 30	48.53 (SD 14.63) <i>n</i> = 101	0.732
3 year eGFR	47.44 (SD 13.90) <i>n</i> = 16	49.71 (SD 14.20) <i>n</i> = 75	0.494

Renal function of ABOi and ABOc transplant recipients

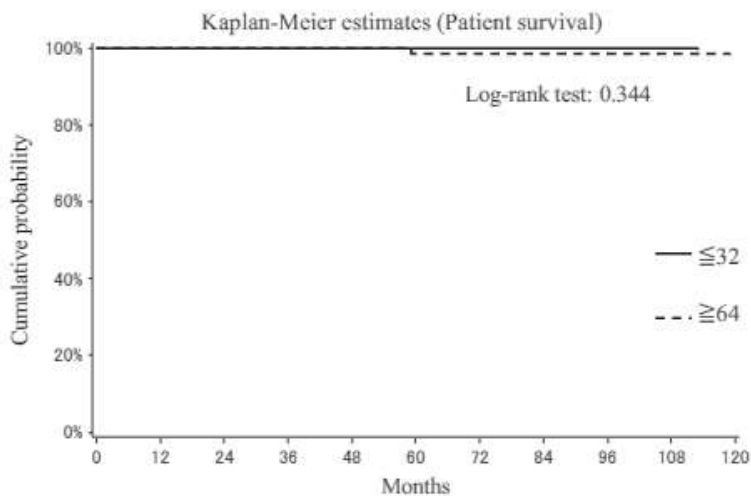
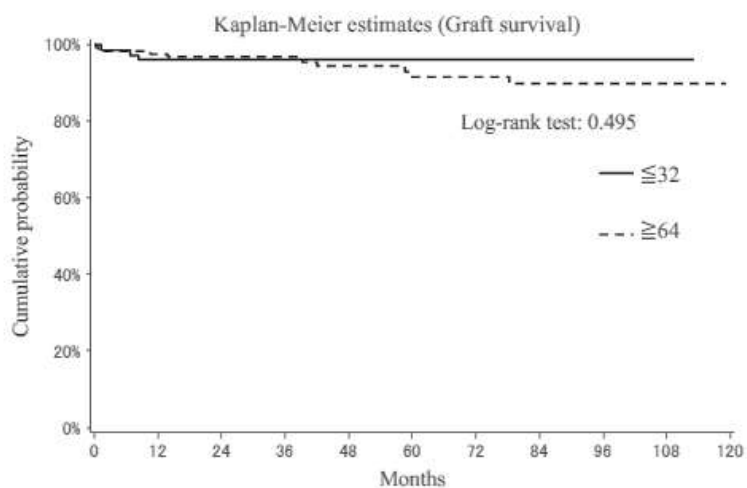
Il trapianto di rene ABO incompatibile: main issues

- ✓ the **minimum 'safe' antibody titer** has not been defined
- ✓ there is **a wide range of assay techniques** available for measuring antibody titers
- ✓ there **is no international standardization of laboratories measuring** anti-A or anti-B antibodies with wide
- ✓ there is debate on **which immunoglobulin subclass** is the potential culprit **leading to hyperacute rejection**
- ✓ the **A1 and B antigens show more intense expression** in kidney than A2, with implications for a potentially higher risk of acute rejection in certain donor–recipient constellations
- ✓ **the clinical relevance of rebounding titers** in the first weeks or even months or years after transplantation **is unknown**

Postoperative rebound of antiblood type antibodies and antibody-mediated rejection after ABO-incompatible living-related kidney transplantation

Hideki Ishida, Tsunenori Kondo, Tomokazu Shimizu, Taiji Nozaki and Kazunari Tanabe

Department of Urology, Kidney Center, Tokyo Women's Medical University, Tokyo, Japan

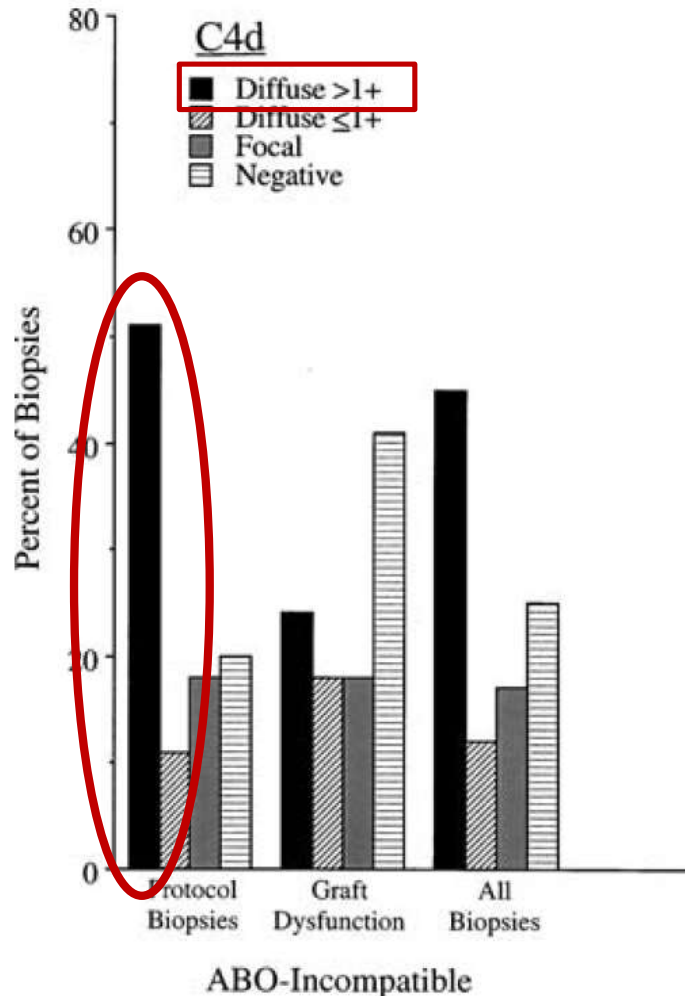


No significant differences **in graft function** at 3 months, 6 months, 1 year, 3 years, 5 years or 10 years between the two groups

No significant statistical differences **in patient and graft survival** rates between the two groups

No significant difference in **any type of graft rejection**

Il trapianto di rene ABO incompatibile: le biopsie di protocollo

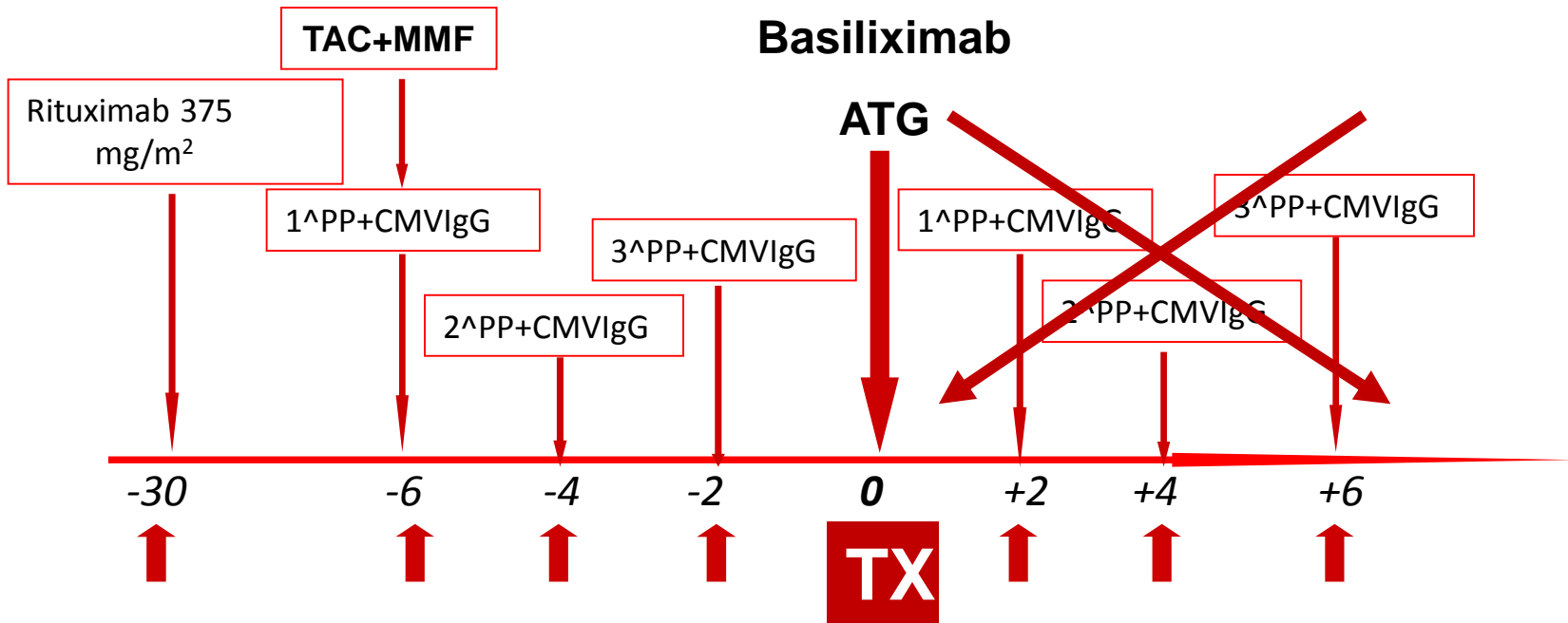


In biopsies of ABO-incompatible renal allografts **C4d deposition in the absence of histologic evidence of rejection is a common finding**, is not associated with an increased risk of graft scarring

The significance of such C4d staining remains a topic of debate, and this finding may have different implications in ABO-incompatible versus conventional renal allografts.

Hass M.; Curr Opin Organ Transplant. 2010 Feb;15(1):21-7

Protocollo di desensibilizzazione



*Monitoraggio isoemoagglutinine
pre e post plasmaferesi*

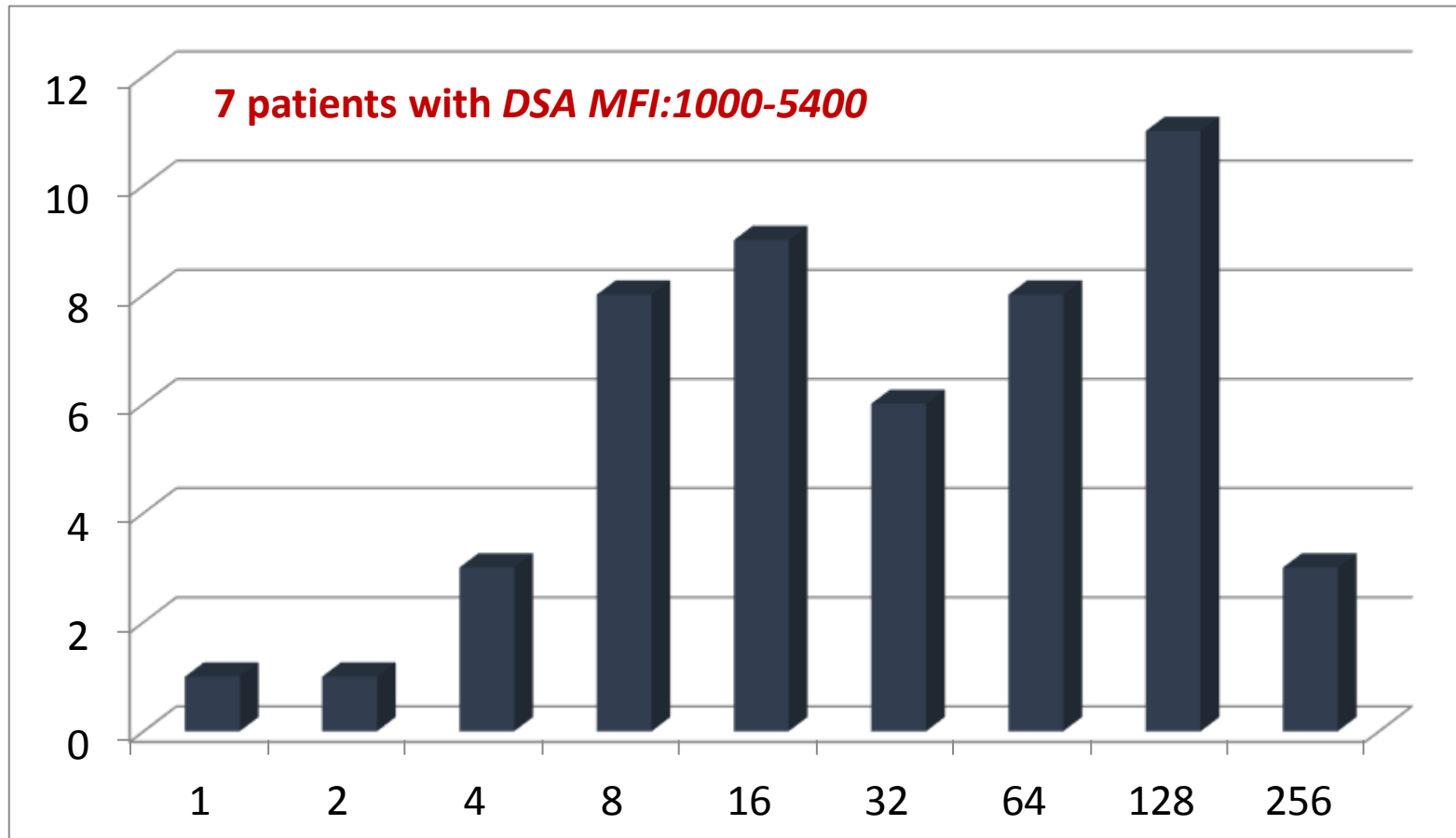
KIDNEY AND PANCREAS TRASPLANTATION UNIT-PADUA

ABO INCOMPATIBLE KIDNEY TRANSPLANT: OUR EXPERIENCE

Determination and monitoring of anti-AB0 antibody titers

Microcolumn agglutination technique

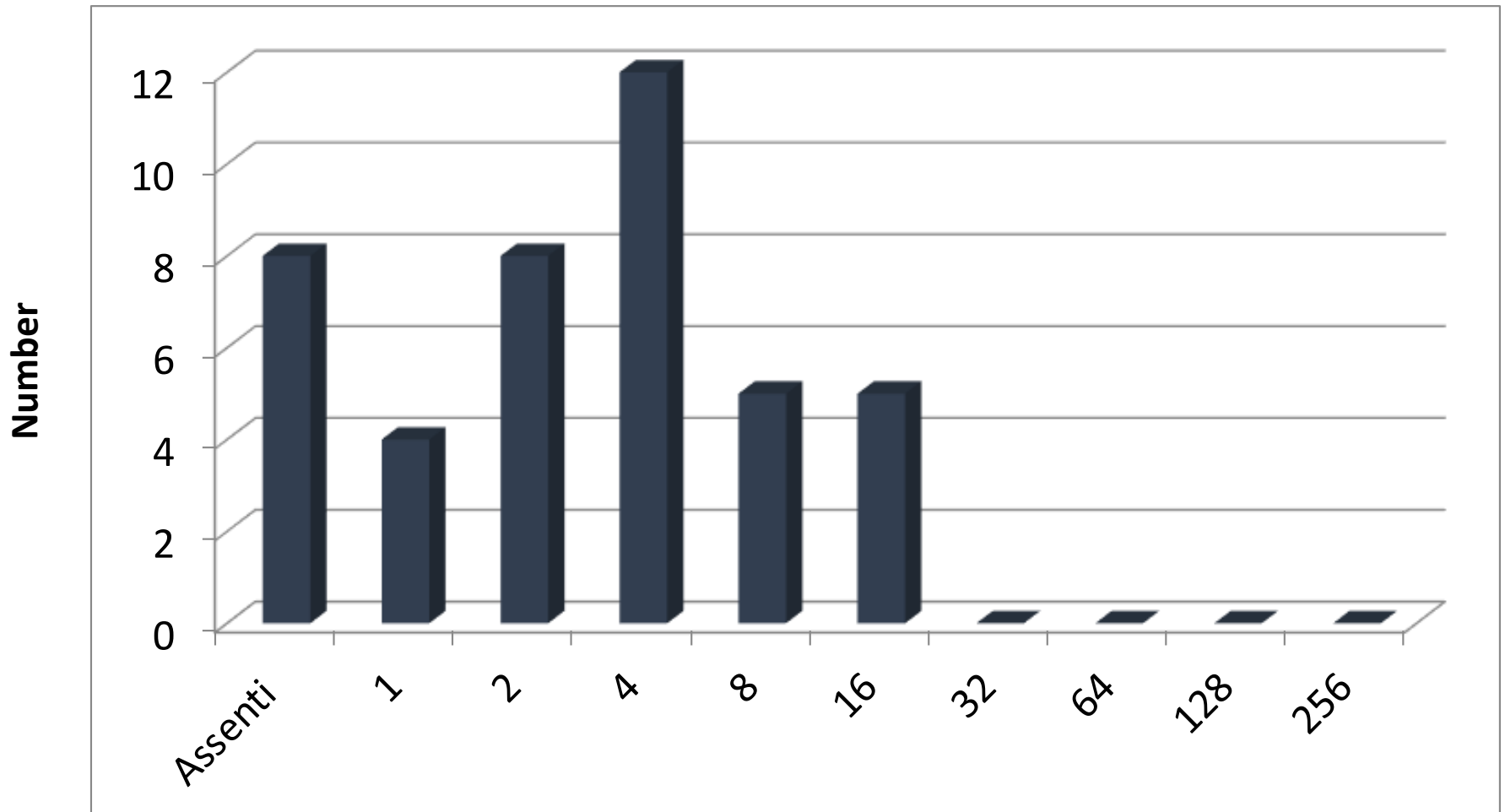
(GEL CARD DIA-MED)



ABOi renal transplant recipients – initial (predesensitization) anti-A/B antibody titers

KIDNEY AND PANCREAS TRASPLANTATION UNIT-PADUA

ABO INCOMPATIBLE KIDNEY TRANSPLANT: OUR EXPERIENCE

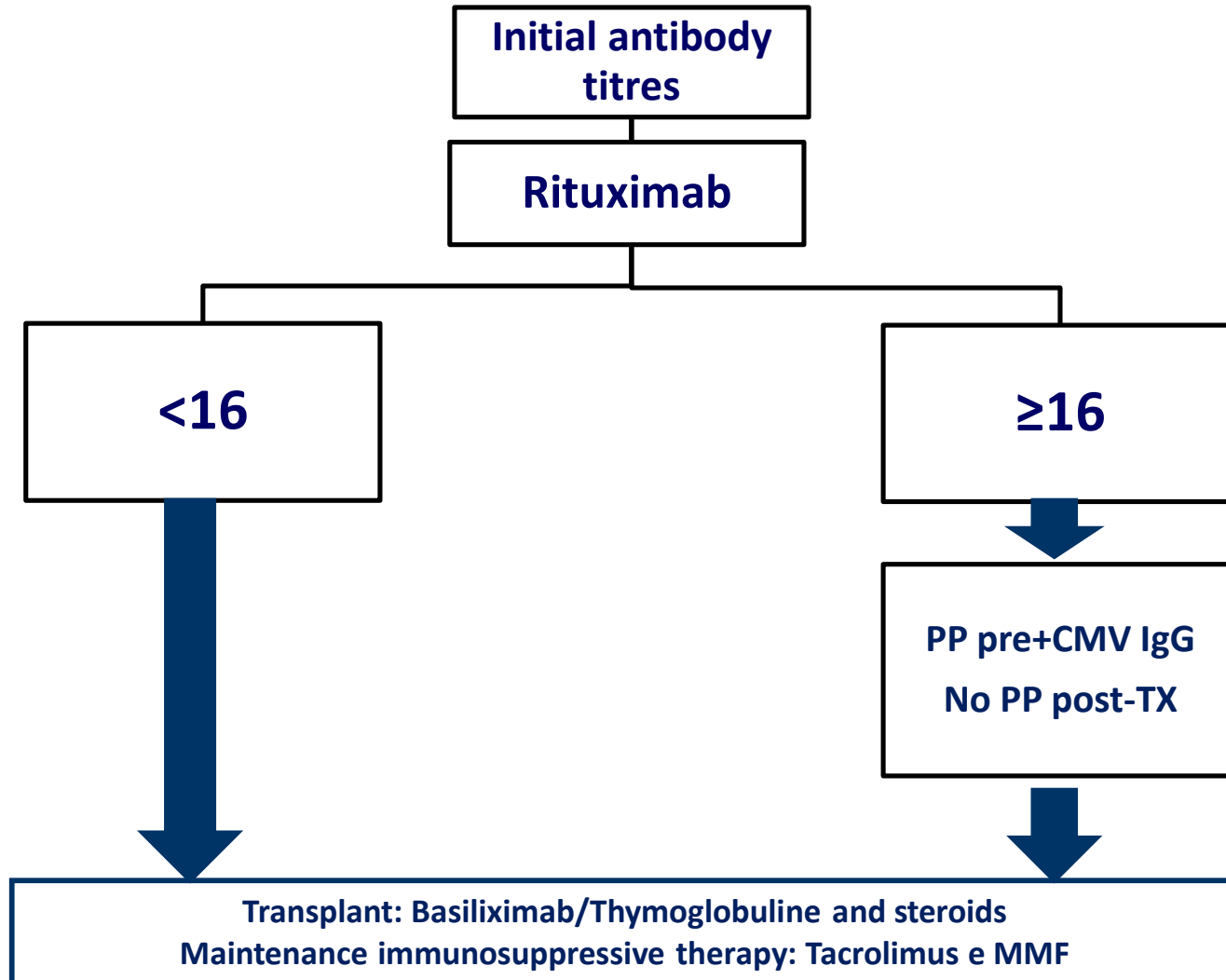


ABOi renal transplant recipients anti-A/B antibody titres at transplant

KIDNEY AND PANCREAS TRANSPLANTATION UNIT-PADUA

ABO INCOMPATIBLE KIDNEY TRANSPLANT: OUR EXPERIENCE

Desensitization Protocol



MONITORING OF ANTI-ABO ANTIBODY TITERS BEFORE AND AFTER TRANSPLANTION

KIDNEY AND PANCREAS TRASPLANTATION UNIT-PADUA

ABO INCOMPATIBLE KIDNEY TRANSPLANT: OUR EXPERIENCE

	Pazienti
Rituximab, PP before and after transplant + CMV IgG/IgVena	24
No Rituximab, PP before and after transplant + CMV IgG	1
Rituximab alone	3
Rituximab, PP+CMV IgG before transplant, PP post-trasplant on demand	17
Rituximab, Therasorb+CMV IgG before and after Tx	3
Rituximab, Glycosorb+CMV IgG before Tx	2



MONITORING OF ANTI-ABO ANTIBODY TITERS BEFORE AND AFTER TRANSPLANTION



NO MORE PROTOCOL BIOPSIES

KIDNEY AND PANCREAS TRASPLANTATION UNIT-PADUA

ABO INCOMPATIBLE KIDNEY TRANSPLANT: OUR EXPERIENCE

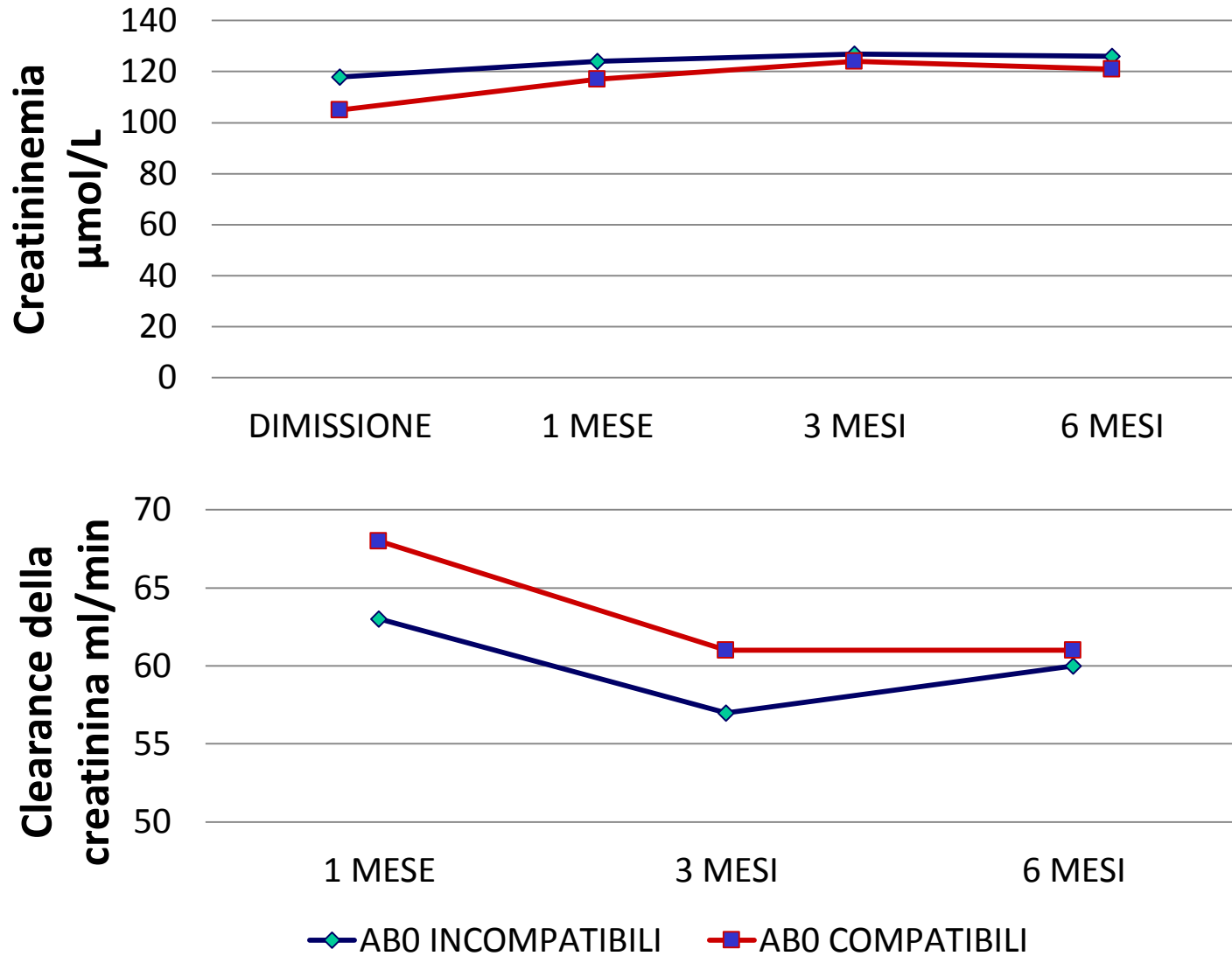
Results

	ABO incompatible	ABO compatible
Patients	50	145
Follow-up (median) (DS)	12 (10.4±13)	26 (28±18.4)
Death	1	0
Graft loss	1	1
DGF	0	1
Duration of DGF (days)	0	6
PNF	0	0
Patients treated for acute rejection (%)	7 (10%)	13 (8.9%)
Trasfusions		
N° patients (%)	10 (20%)	17 (14.9%)
Lenght of hospital stay (days)	15 (13-16)	12 (11-14)

KIDNEY AND PANCREAS TRANSPLANTATION UNIT-PADUA

ABO INCOMPATIBLE KIDNEY TRANSPLANT: OUR EXPERIENCE

Renal Function



KIDNEY AND PANCREAS TRASPLANTATION UNIT-PADUA

ABO INCOMPATIBLE KIDNEY TRANSPLANT: OUR EXPERIENCE

Complications

	ABO incompatible	ABO compatible	p-value
Patients	50	145	
SURGICALS			
Bleeding	1 (2%)	1 (0.68%)	-
Hematoma	0	1 (0.68%)	-
Lymphocele	1 (2%)	1 (0.68%)	-
Wound dehiscence	0	1 (0.68%)	-
Bowel obstruction	0	1 (0.68%)	-
INFECTIONS			
CMV	3 (6%)	6 (4.13%)	0.62
BK	1 (2%)	3 (2.06%)	0.54
Pyelonephritis	0	2 (1.37%)	-
Pneumonia	0	1 (0.68%)	-
Cellulite	1 (2%)	1 (0.68%)	0.30
MEDICAL			
PTDM	0	6 (4.13 %)	0.58
Leukopenia	2 (4%)	3 (2.06%)	0.20
PTLD	0	1 (0.68%)	-

CONCLUSIONI

- ✓ I **RISULTATI** OTTENUTI DAI TRAPIANTI DI RENE DA DONATORE VIVENTE ABO INCOMPATIBILE SONO OTTIMI E PARAGONABILI A QUELLI OTTENUTI NEI TRAPIANTI DI RENE DA DONATORE VIVENTE ABO COMPATIBILE
- ✓ IL PROTOCOLLO DI **DESENSIBILIZZAZIONE** BASATO SU RITUXIMAB, PLASMAFERESI E CMV-IgG SPECIFICHE SI È DIMOSTRATO EFFICACE E SICURO
- ✓ LA TENDENZA GENERALE SEMBRA UNA RIDUZIONE DEI PROTOCOLLI DI DESENSIBILIZZAZIONE
- ✓ IL PROGRAMMA DI TRAPIANTO ABO INCOMPATIBILE HA PERMESSO DI AUMENTARE IL NUMERO DI TRAPIANTI DA DONATORE VIVENTE

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