Enhancing Success and Quality of Life in ABO-Incompatible Kidney Transplantation: the Padova Experience

Anna Colpo, MD

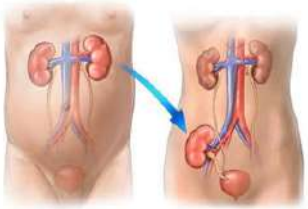
Therapeutic Apheresis Unit

Department of Transfusion Medicine

Padova University Hospital, Italy

Athens, 27th november 2025

ABOi kidney transplantation: starting point



Key points

- ABO-incompatible (ABOi) kidney transplantation is now an established treatment option for patients with end-stage renal disease, but the mechanisms that underlie acceptance of ABOi grafts are not well understood
- The biology of the ABO system is complex; blood group subtypes and organ-specific patterns of core-chain tissue distribution require particular consideration in the context of ABOi transplantation
- Innovative humanized animal models are expected to provide a better understanding of anti-A/B immune responses and might help to establish innovative therapeutic strategies to counteract blood-group-specific B-cell responses
- The development of efficient desensitization protocols including apheresis, modulation of B-cell immunity and long-term maintenance immunosuppression has enabled ABOi kidney transplantation to become a safe treatment strategy with favourable outcomes
- Although the reduction of pretransplant anti-A/B antibody titres below a permissive threshold is a major principle of desensitization, thresholds at which antibody-mediated damage can be predicted have not been defined
- Tailoring the intensity of preconditioning for ABOi kidney transplant recipients according to their pretransplant anti-A/B antibody titres might be an efficient strategy to minimize the risks associated with enhanced immunosuppression

A and B blood antigens are expressed on the endothelium and epithelial cells of the kidney

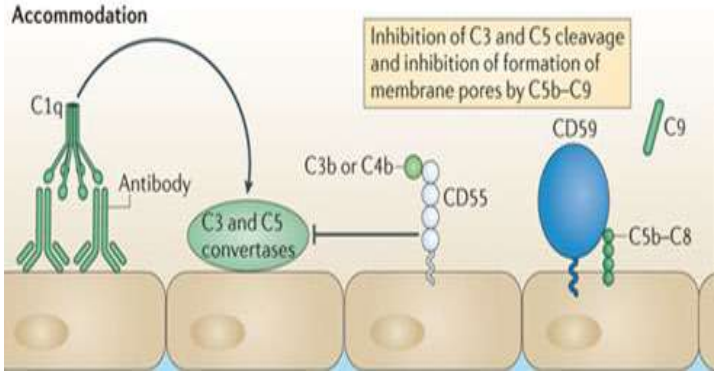
Böhmig, et al. Nat. Rev. Nephrol 2015

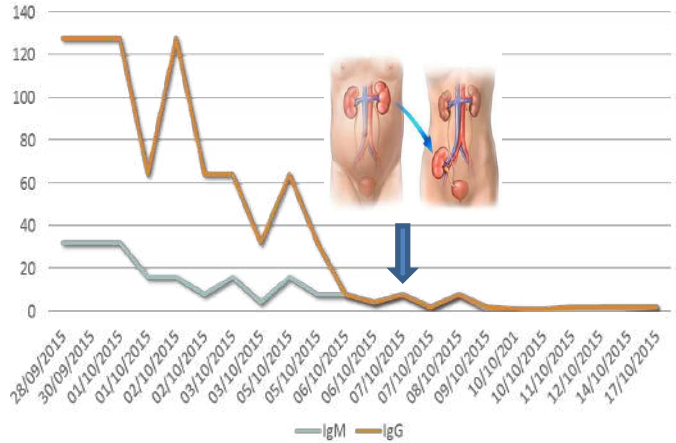
Desensitization: rationale in ABOi kidney transplantation

Accomodation is an acquired resistance of an organ graft to humoral injury and rejection, developed in 2/4 weeks in the presence of low titers antibodies.

It is the phenomenon of continuing survival of an ABO-incompatible graft despite the presence of ABO antibodies.

Grafts acquire a higher level of resistance to injury by antibodies and complement. This resistance reflects in part the repair of damage already inflicted and in part changes at the cellular and tissue level that reduce susceptibility to injury.





Trends in Anti-A/B antibodies titers during desensitization and after ABOi KTX

ABOi kidney transplantation: international experiences

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

Takahashia K et al., AJT 2004

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

Sonnenday C.J. et al., AJT 2004

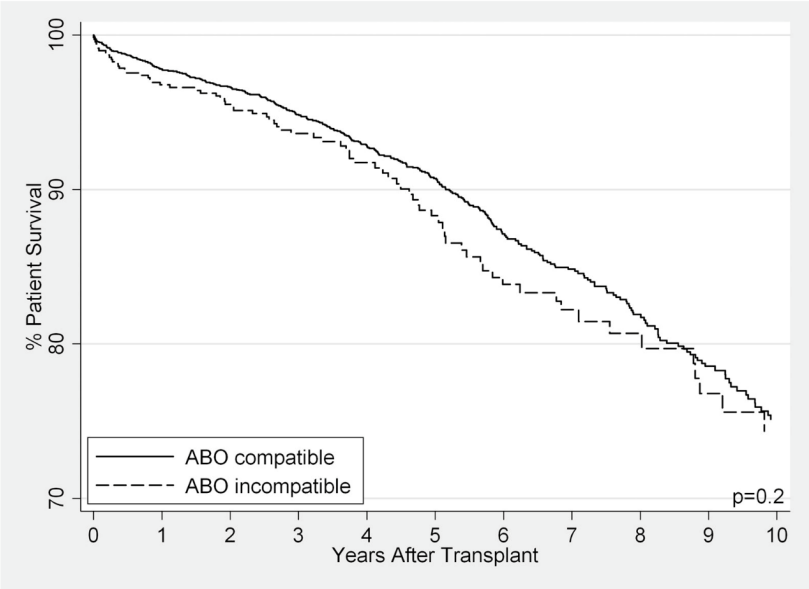
ABO Incompatible Kidney Transplantations Without Splenectomy, Using Antigen-Specific Immunoadsorption and Rituximab

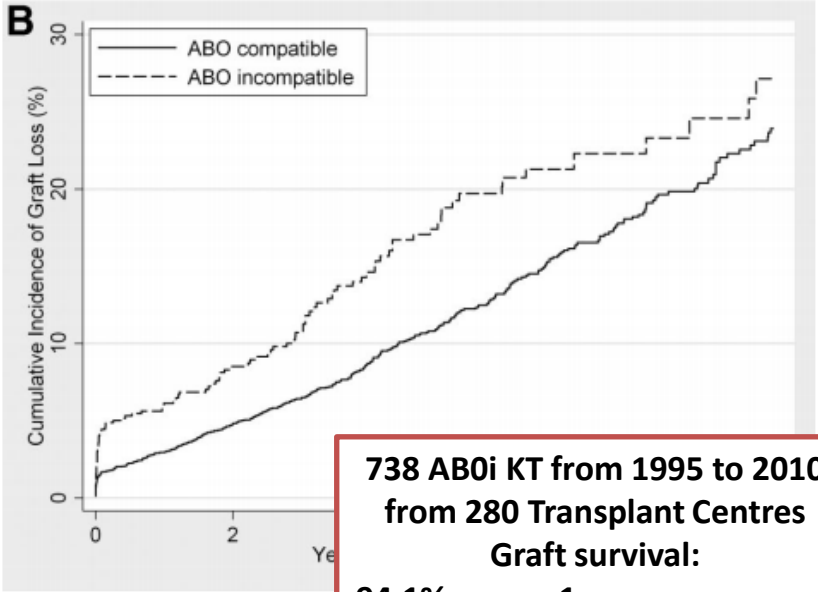
Tyden G et al., AJT 2005

ABO-Incompatible Kidney Transplantation Using Antigen-Specific Immunoadsorption and Rituximab: A 3-Year Follow-up

Genberg et al., Transplantation 2008

ABOi kidney transplantation: the American experience





738 AB0i KT from 1995 to 2010 from 280 Transplant Centres

Graft survival:

94.1%	**1 year**
89.6%	**3 years**
82.6%	**5 years**
72.9%	**10 years**

- comparable patient survival
- higher graft loss for ABOi KTx particularly in the first 14 days
- similar results in the centers regardless the number of procedures for each center, suggesting a minimal *learning curve*

Montgomery et al. Transplantation 2012

ABOi kidney transplantation: the American experience

CLINICAL AND TRANSLATIONAL RESEARCH

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 Haas[2]

After transplantation, TPE therapy is performed for all patients to prevent rebound of anti-A and anti-B titers until accommodation occurs.

TABLE 1. The number of planned pre- and posttransplant PP/IVIg treatments correlate with the starting isohemagglutinin titer

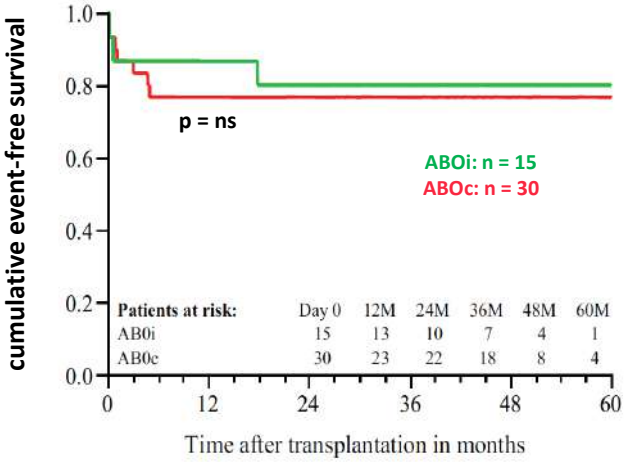
Starting isoagglutinin AHG titer	Pretransplant PP/IVIG treatments	Posttransplant PP/IVIG treatments
<16	2	2
16–32	3	2–3
64	4	3
128	5–6	4
256	7–8	4
512	9–10	5
>512	>10	6

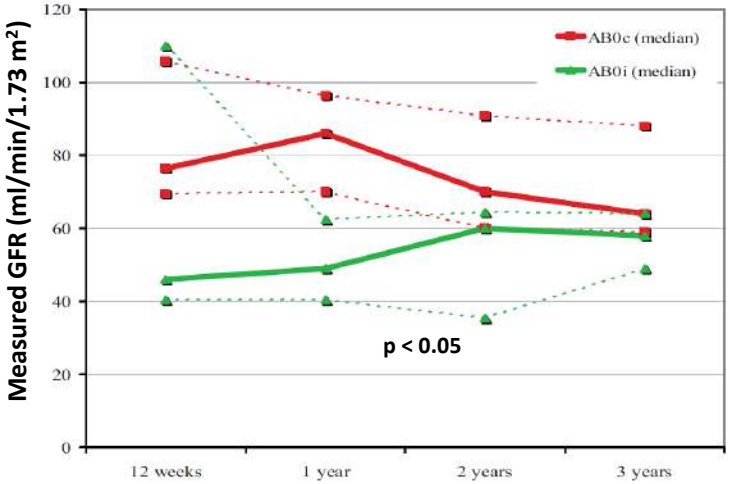
PP, plasmapheresis; AHG, anti-human globulin.

Montgomery et al. Transplantation 2009

ABOi kidney transplantation: the Swedish experience

Desensitization with Rituximab + antigen-specific immunoadsorption + IV-IgG
years 2000 - 2005

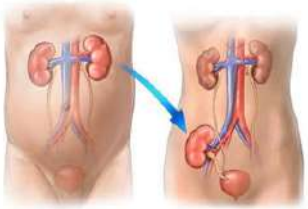




- comparable patient and graft survival and rejection rate
- no increased incidence of infections or other complications
- Protocol expanded to other North Europe centers with favorable outcome

Genberg et al. Transplantation 2008

ABOi kidney transplantation: starting point



Key points

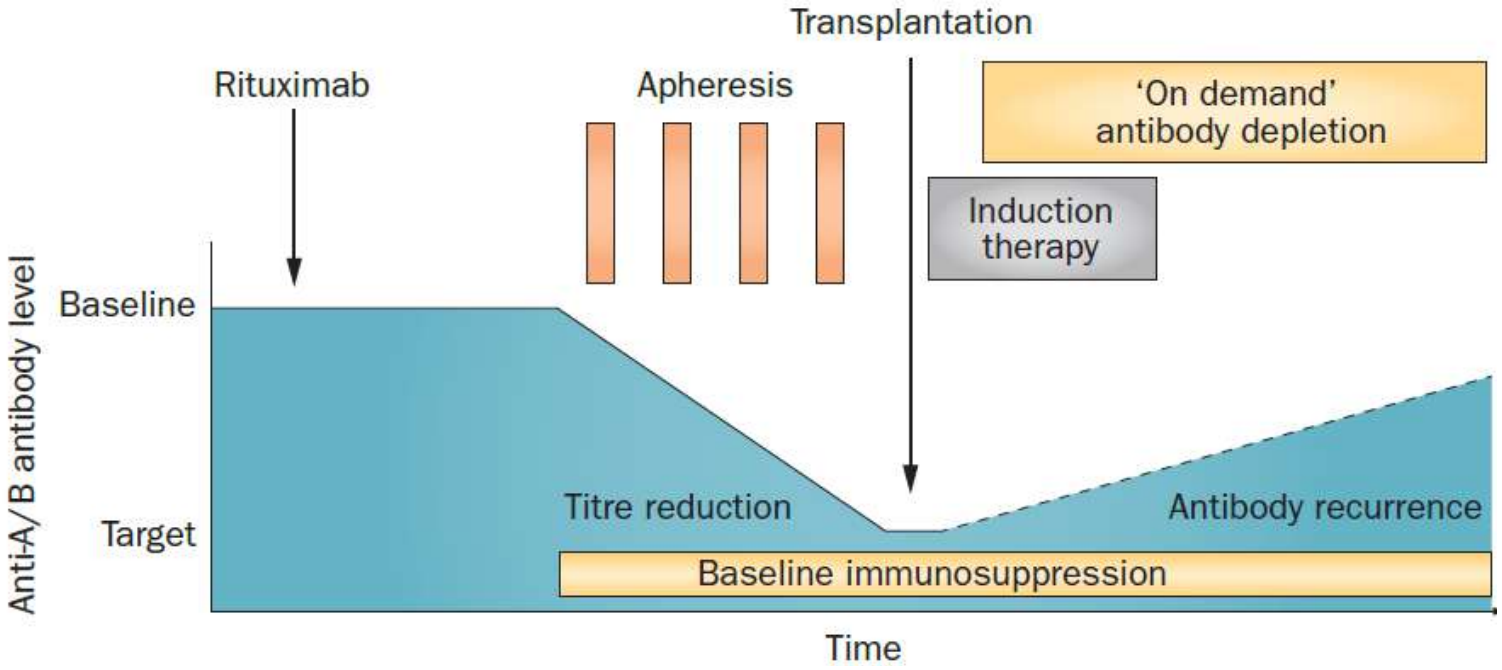
- ABO-incompatible (ABOi) kidney transplantation is now an established treatment option for patients with end-stage renal disease, but the mechanisms that underlie acceptance of ABOi grafts are not well understood
- The biology of the ABO system is complex; blood group subtypes and organ-specific patterns of core-chain tissue distribution require particular consideration in the context of ABOi transplantation
- Innovative humanized animal models are expected to provide a better understanding of anti-A/B immune responses and might help to establish innovative therapeutic strategies to counteract blood-group-specific B-cell responses
- The development of efficient desensitization protocols including apheresis, modulation of B-cell immunity and long-term maintenance immunosuppression has enabled ABOi kidney transplantation to become a safe treatment strategy with favourable outcomes
- Although the reduction of pretransplant anti-A/B antibody titres below a permissive threshold is a major principle of desensitization, thresholds at which antibody-mediated damage can be predicted have not been defined
- Tailoring the intensity of preconditioning for ABOi kidney transplant recipients according to their pretransplant anti-A/B antibody titres might be an efficient strategy to minimize the risks associated with enhanced immunosuppression

Böhmig, et al. Nat. Rev. Nephrol 2015

Key elements of desensitization in ABOi KT

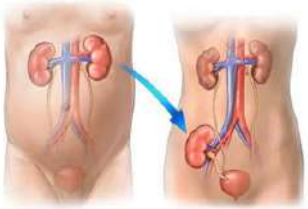
Antibodies removal	B Lymphocytes depletion	Immuno suppression/ modulation
THERAPEUTIC APHERESIS	*(SPLENECTOMY)* **RITUXIMAB**	**INDUCTION and MAINTENANCE DRUGS IVIg**

Key elements of desensitization in ABOi KT



Böhmig, et al. Nat. Rev. Nephrol 2015

ABOi kidney transplantation: starting point



Key points

- ABO-incompatible (ABOi) kidney transplantation is now an established treatment option for patients with end-stage renal disease, but the mechanisms that underlie acceptance of ABOi grafts are not well understood
- The biology of the ABO system is complex; blood group subtypes and organ-specific patterns of core-chain tissue distribution require particular consideration in the context of ABOi transplantation
- Innovative humanized animal models are expected to provide a better understanding of anti-A/B immune responses and might help to establish innovative therapeutic strategies to counteract blood-group-specific B-cell responses
- The development of efficient desensitization protocols including apheresis, modulation of B-cell immunity and long-term maintenance immunosuppression has enabled ABOi kidney transplantation to become a safe treatment strategy with favourable outcomes
- Although the reduction of pretransplant anti-A/B antibody titres below a permissive threshold is a major principle of desensitization, thresholds at which antibody-mediated damage can be predicted have not been defined
- Tailoring the intensity of preconditioning for ABOi kidney transplant recipients according to their pretransplant anti-A/B antibody titres might be an efficient strategy to minimize the risks associated with enhanced immunosuppression

Böhmig, et al. Nat. Rev. Nephrol 2015

ABOi kidney transplantation: minimization strategies

✓ Rituximab	→	When? Dosage?
✓ Pre-transplant apheresis	→	According to initial anti-A/B titres
✓ Non selective TA	→	Selective TA treatments
✓ Post-transplant apheresis	→	On demand strategy
✓ Apheresis+dyalisis	→	TANDEM procedure

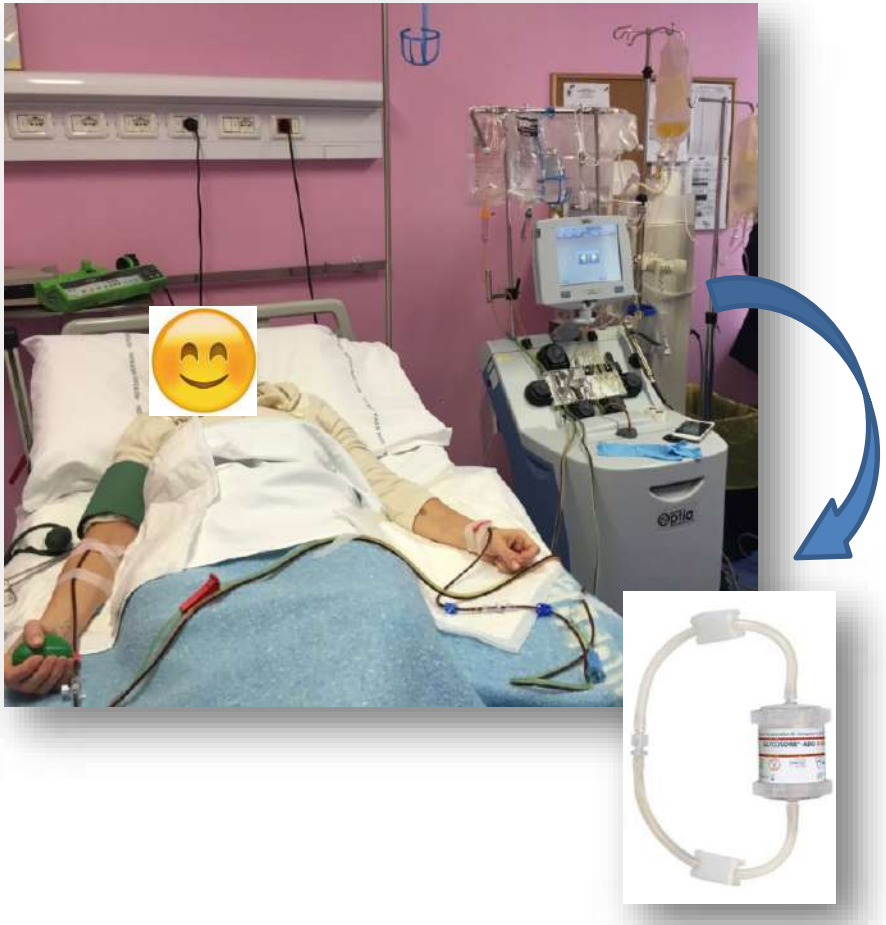
Advantages of minimization: reduced morbidity and costs

Therapeutic apheresis in desensitization

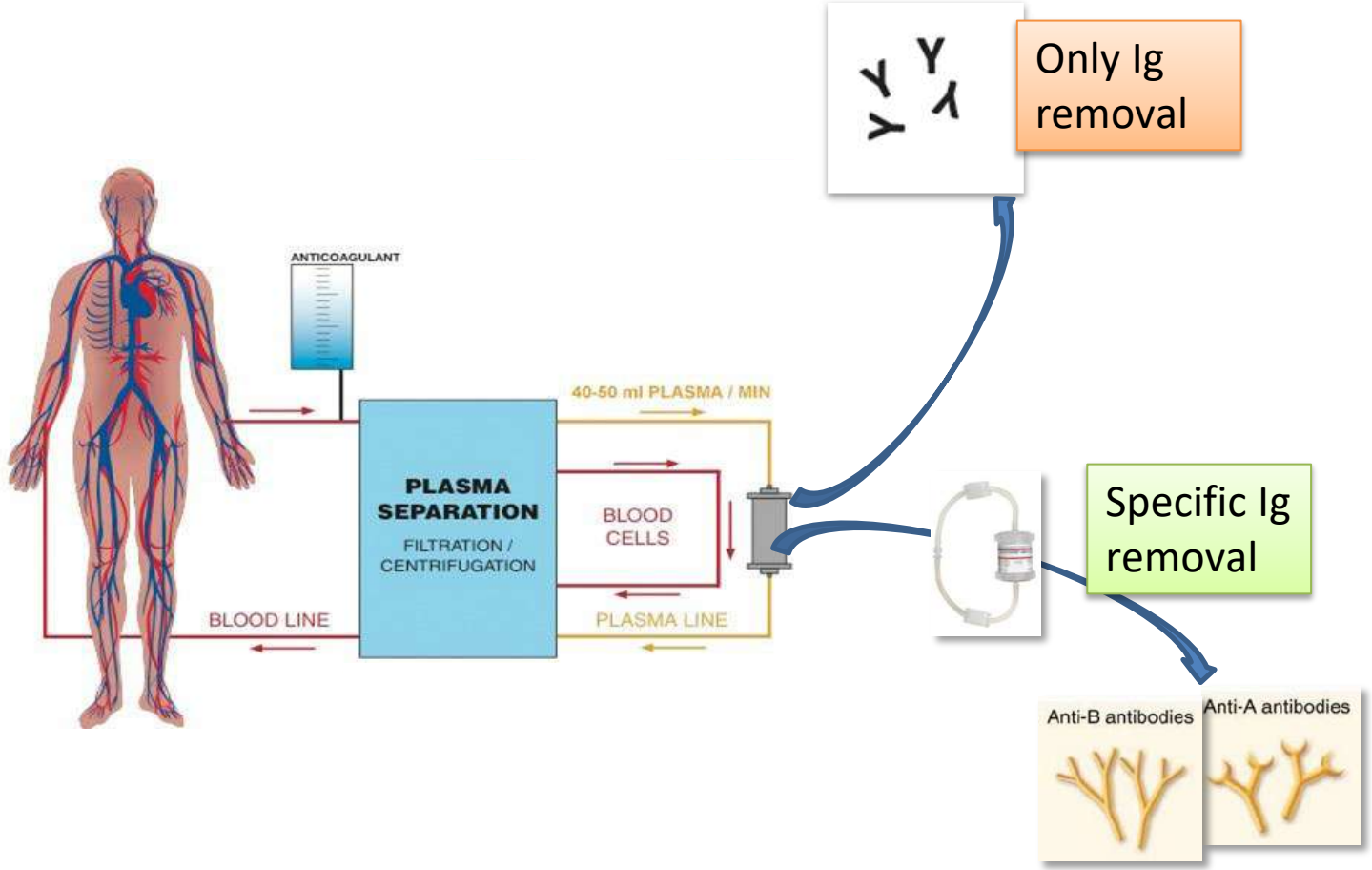
TPE	DFPP/CF	IA	ABO-IA
• Non selective • 1-1,5 plasma processing volumes • Substitution fluids: albumin/FFP • Removes all plasma components *(coagulation factors!)* • Easy to use and promptly avalilable • Cheaper than other techniques • *Less efficient*	• Semiselective • 1-2 plasma processing volumes • No need for any substitution fluids • Removes macromolecules	• Selective • ≥ 2-3 plasma processing volumes • No need for any substitution fluids • Removes Ig	• “Super” selective • ≥ 2-3 plasma processing volumes • No need for any substitution fluids • Removes only ABO antibodies • Preservation of overall immunoglobulin function • Reduced infection risk • *More expensive than other techniques*

Super selective IA: Glycosorb ABO

The most selective TA technique is the ABO-specific IA. The Glycosorb ABO columns are ABO-specific adsorbers that have been developed by a Swedish biotech company
and contains synthetic terminal trisaccharides from A
or B (or both) ABO blood group antigen covalently bound to
Sepharose matrix.



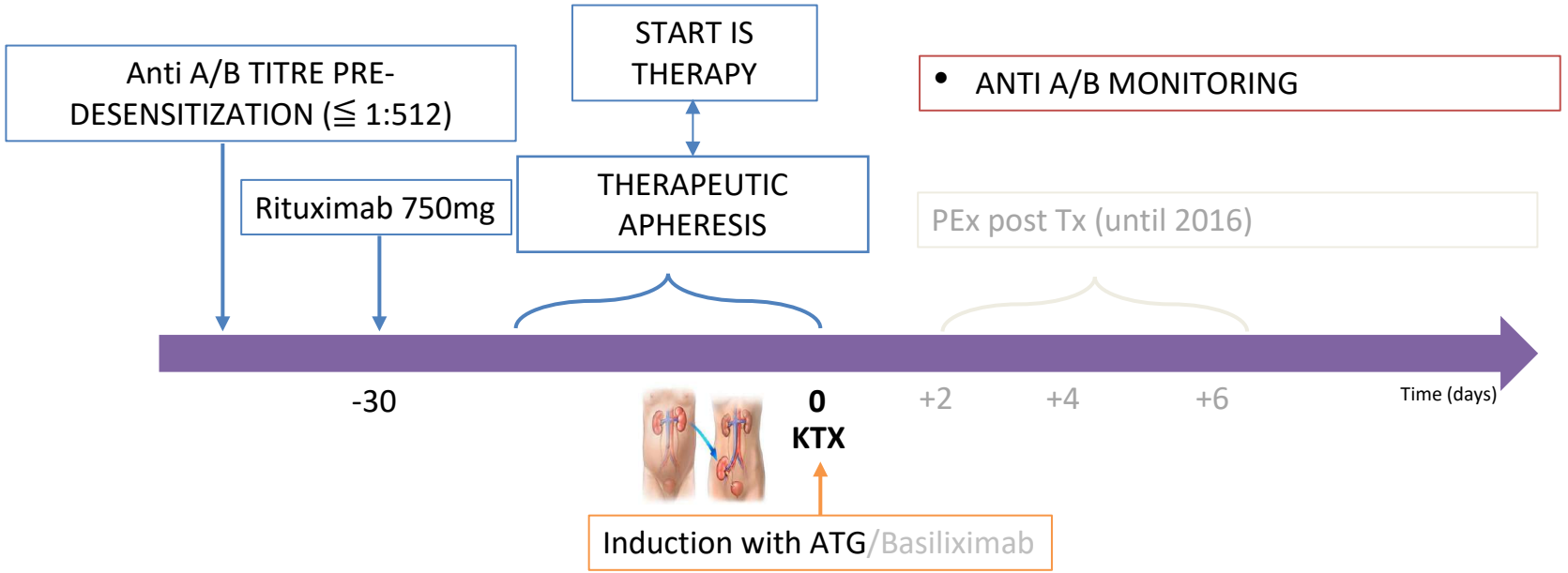
Immunoadsorption in ABOi kidney transplantation



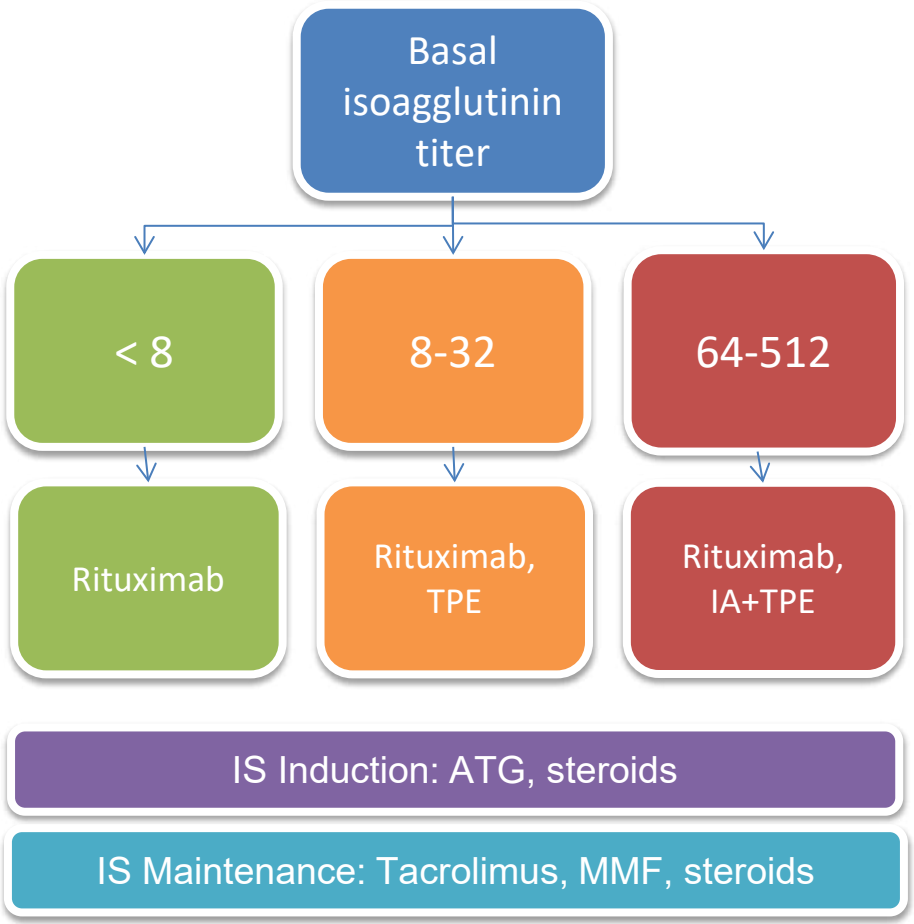
Desensitization in ABOi kidney transplant

A tailored therapy: each patients should have a customized desensitization plan

ABOi kidney transplantation: the *Padova protocol*



ABOi kidney transplantation: the *Padova protocol*

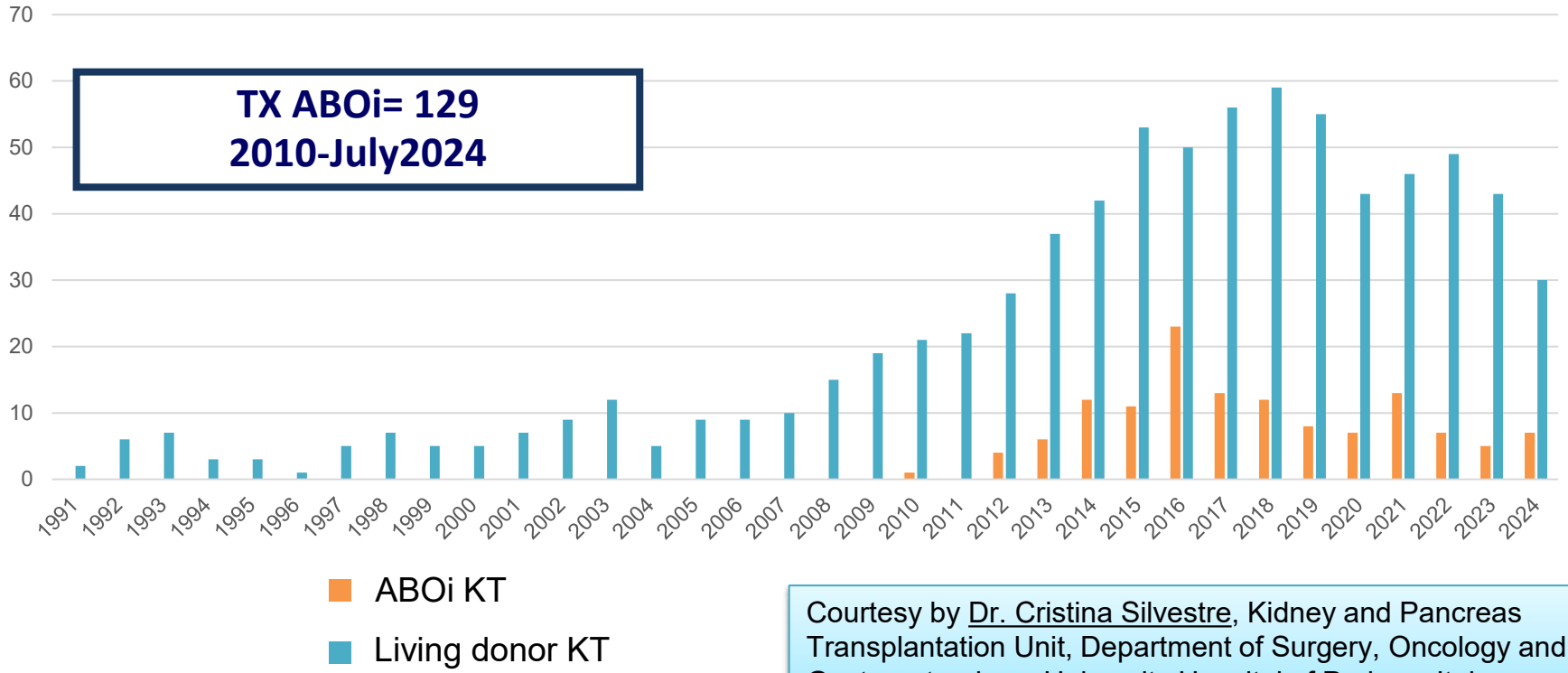


Target titer ≦ 8

The definite number of TPE and IA sessions depends on basal titer and on antibody titre trend during desensitization (i.e. rebound)

In higher titers the approach is always combined

ABOi kidney transplantation: *Padova*

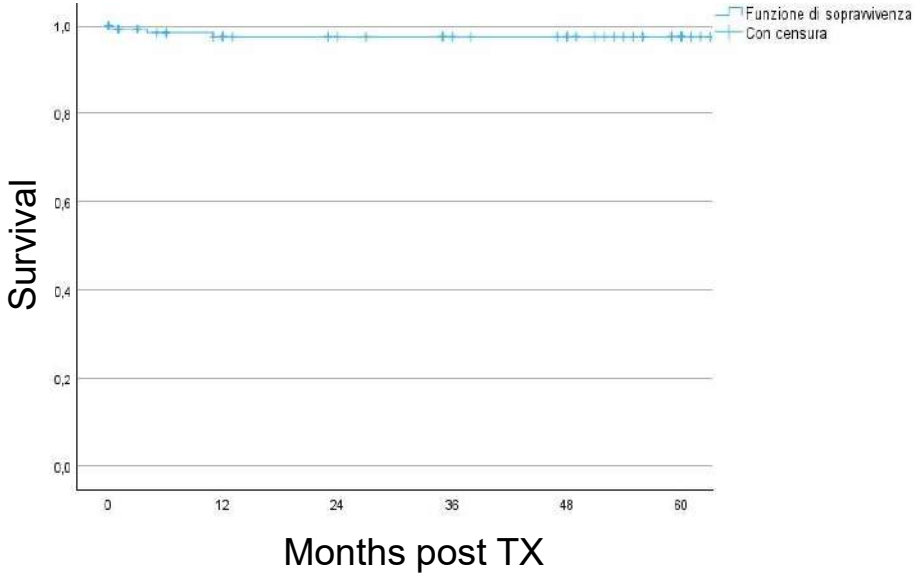


Courtesy by Dr. Cristina Silvestre, Kidney and Pancreas Transplantation Unit, Department of Surgery, Oncology and Gastroenterology, University Hospital of Padova, Italy

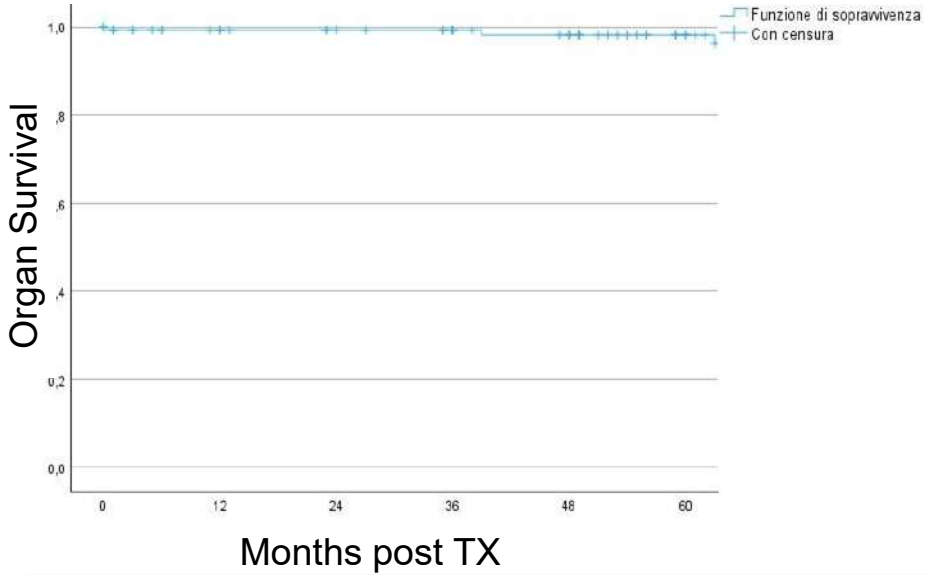
ABOi kidney transplantation: *Padova*

REGIONE DEL VENETO
Azienda Ospedale Università Padova

Patient Survival



Graft Survival

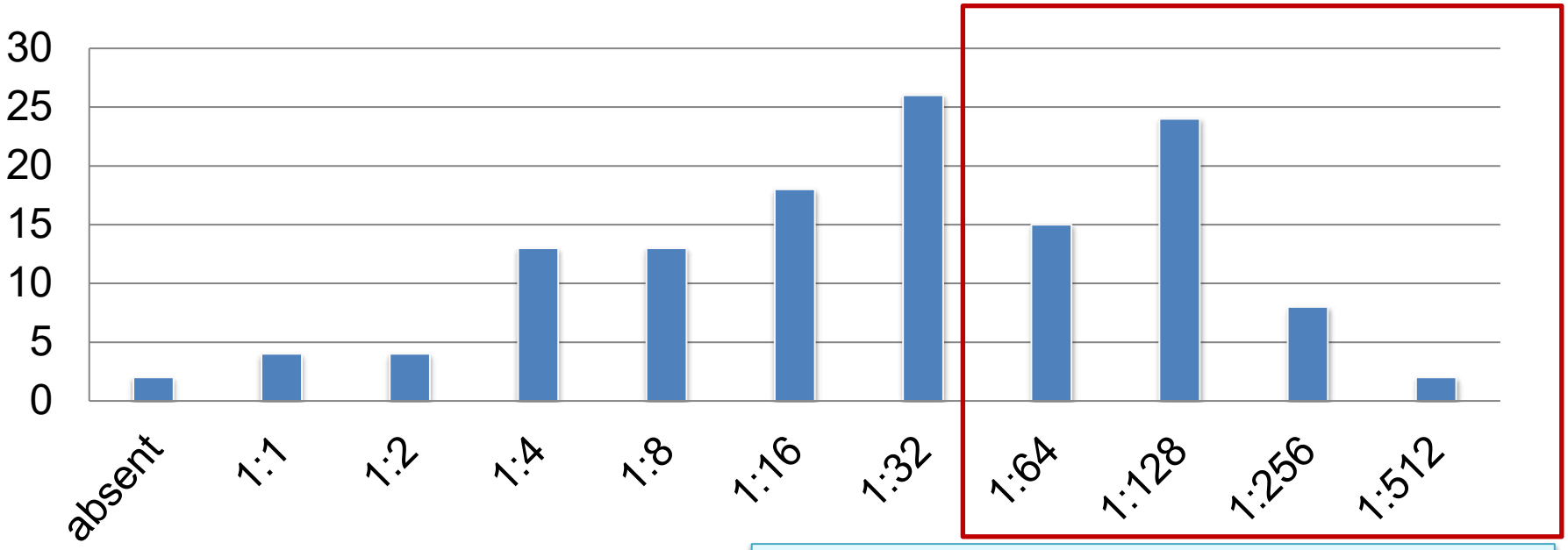


Courtesy by Dr. Cristina Silvestre, Kidney and Pancreas Transplantation Unit, Department of Surgery, Oncology and Gastroenterology, University Hospital of Padova, Italy

ABOi kidney transplantation: *Padova*

REGIONE DEL VENETO
Azienda Ospedale Università Padova

Anti A/B titre pre desensitization

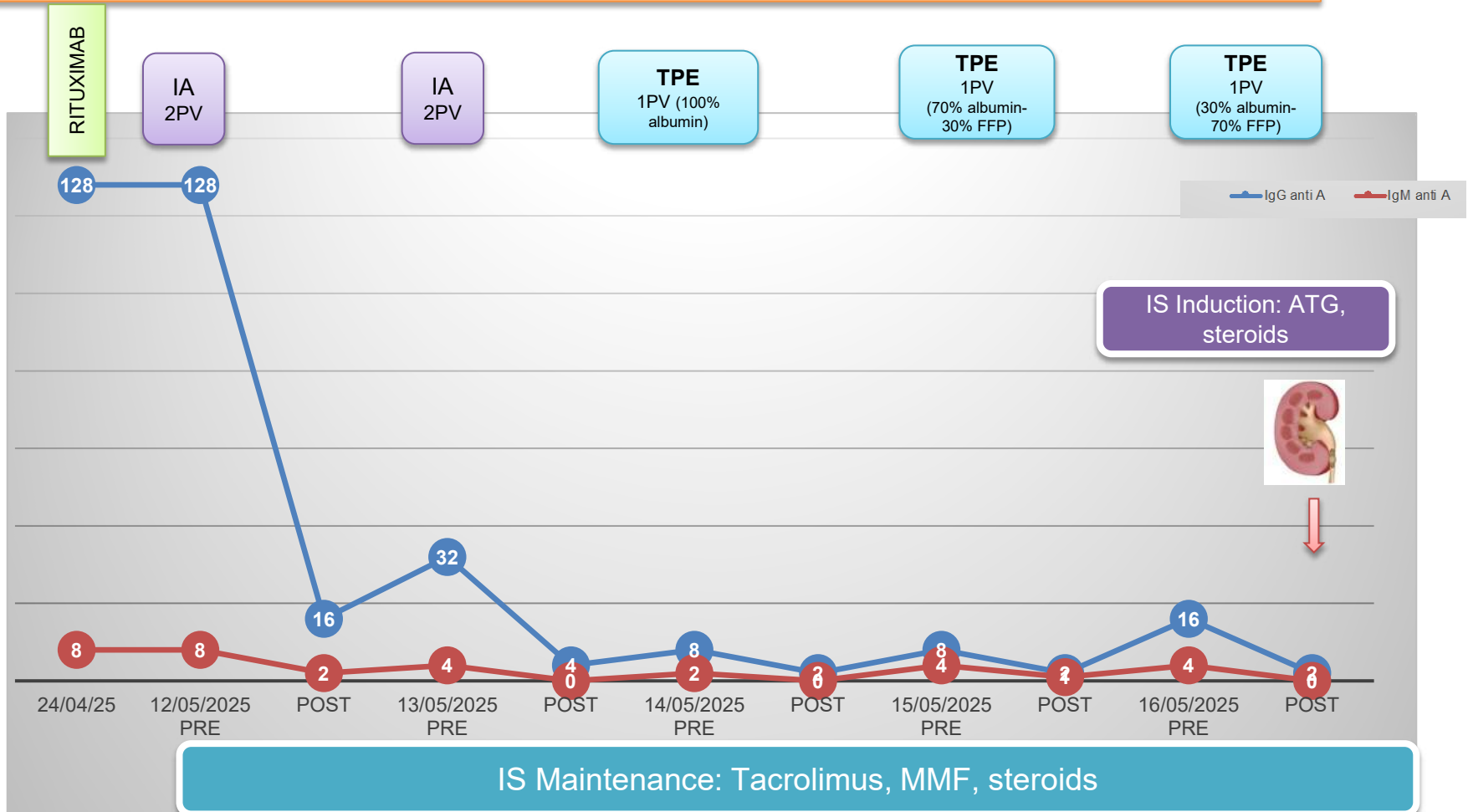


Courtesy by Dr. Cristina Silvestre, Kidney and Pancreas Transplantation Unit, Department of Surgery, Oncology and Gastroenterology, University Hospital of Padova, Italy

Therapeutic apheresis in ABOi kidney transplant: *Padova experience*

Pt	Sex	Date of Tx	Renal Replacement Therapy	Date of Rituximab	Donor/ recipient ABO inc.	Isoagglutinin titers			Number of Apheresis sessions	Immuno suppression	Adverse events	Acure rejection	Apheresis post Tx	Serum creatinine @discharge	Isoagglutinin titer @ last FU	Late complications
						Before apheresis	Pre Tx	@discharge								
7	M	30/07/2025	pre-emptive	26/08/2025	A/O	256	16	64	3 IA, 3 TPE	MMF, tacro, ATG, steroids, **eculizumab**	NO	YES	yes, 3 TPE + eculizumab	190	32	/
6	F	16/05/2025	HD	23/04/2025	A/O	128	4	8	2 IA, 3 TPE	MMF, tacro, ATG, steroids	NO	NO	NO	50	4	/
5	M	27/06/2025	HD	17/04/2025	A/O	256	8	32	3 IA, 2 TPE	MMF, tacro, ATG, steroids, **eculizumab**	NO	NO	NO	119	16	/
4	M	18/10/2024	pre-emptive	18/09/2024	A/O	512	4	32	5 IA, 1 TPE	MMF, tacro, ATG, steroids	NO	YES	yes, 3 TPE + eculizumab	105	64	Pneumonia
3	M	07/05/2024	pre-emptive	17/04/2024	A/O	256	4	16	3 IA, 3 TPE	MMF, tacro, ATG, steroids	NO	NO	yes, 2 TPE	147	128	/
2	M	13/10/2023	PD	18/09/2023	A/O	64	4	4	1 IA, 1 TPE	MMF, tacro, ATG, steroids	NO	NO	NO	105	2	Pneumonia, FSGS
1	F	28/05/2021	HD	04/05/2021	A/O	64	2	1	2 IA, 1 TPE	MMF, tacro, ATG, steroids	NO	NO	NO	374	2	post op hemorrage

Therapeutic apheresis in ABOi kidney transplant: *Padova experience*

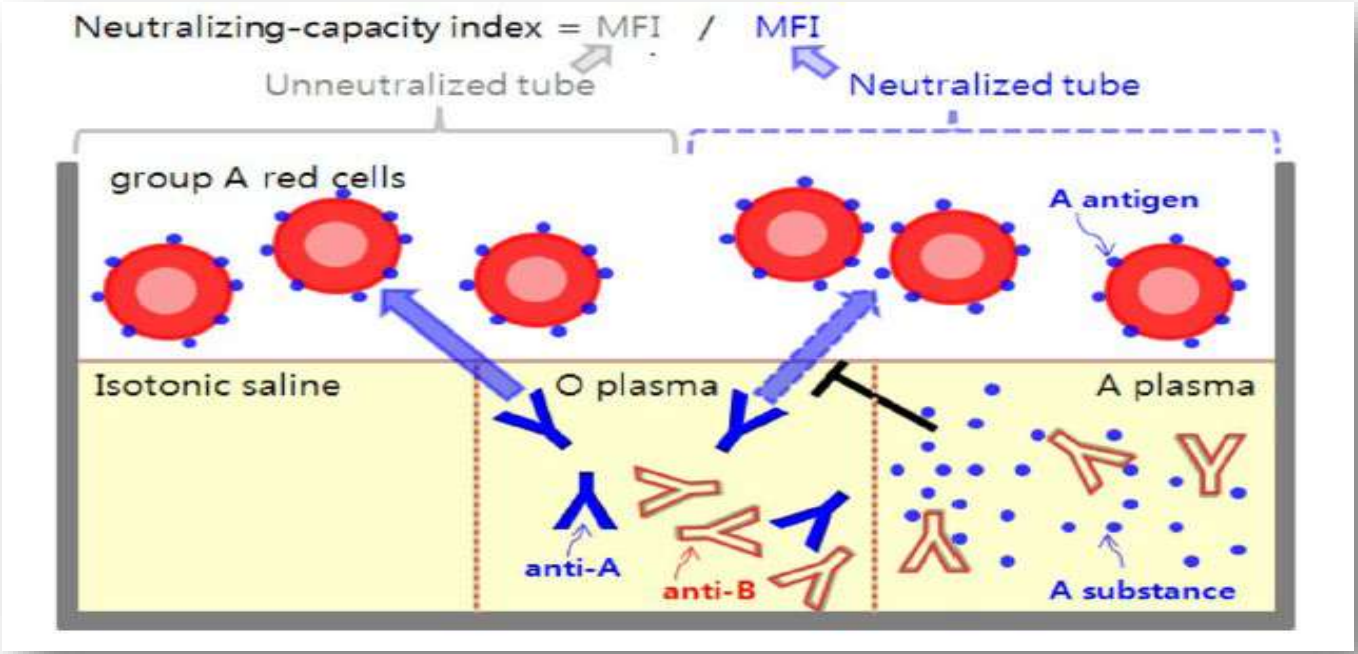


Therapeutic apheresis in ABOi kidney transplantation

2015;30:288-296

Benefits of Fresh-Frozen Plasma as a Replacement Fluid to Neutralize ABO Antibodies

Dong Il Won,[1]* Ji Yeon Ham,[1] Chan Duck Kim,[2] Jang Soo Suh,[1] and Byung Chang Kim[3]

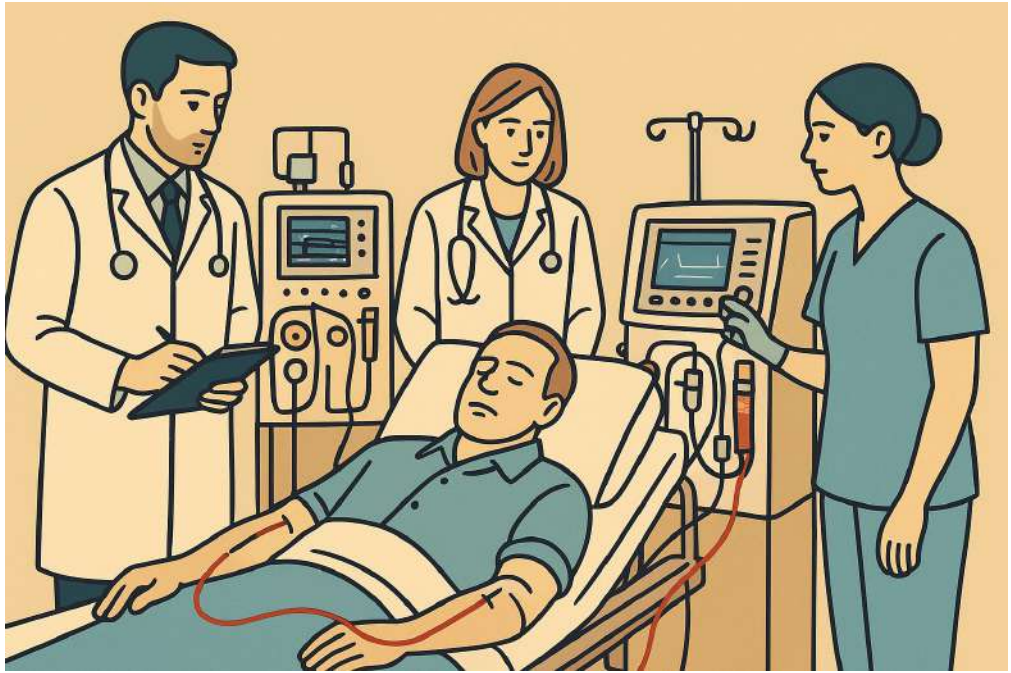


Tandem Apheresis – HD Approach

Rationale: optimize patient time, hemodynamic stability

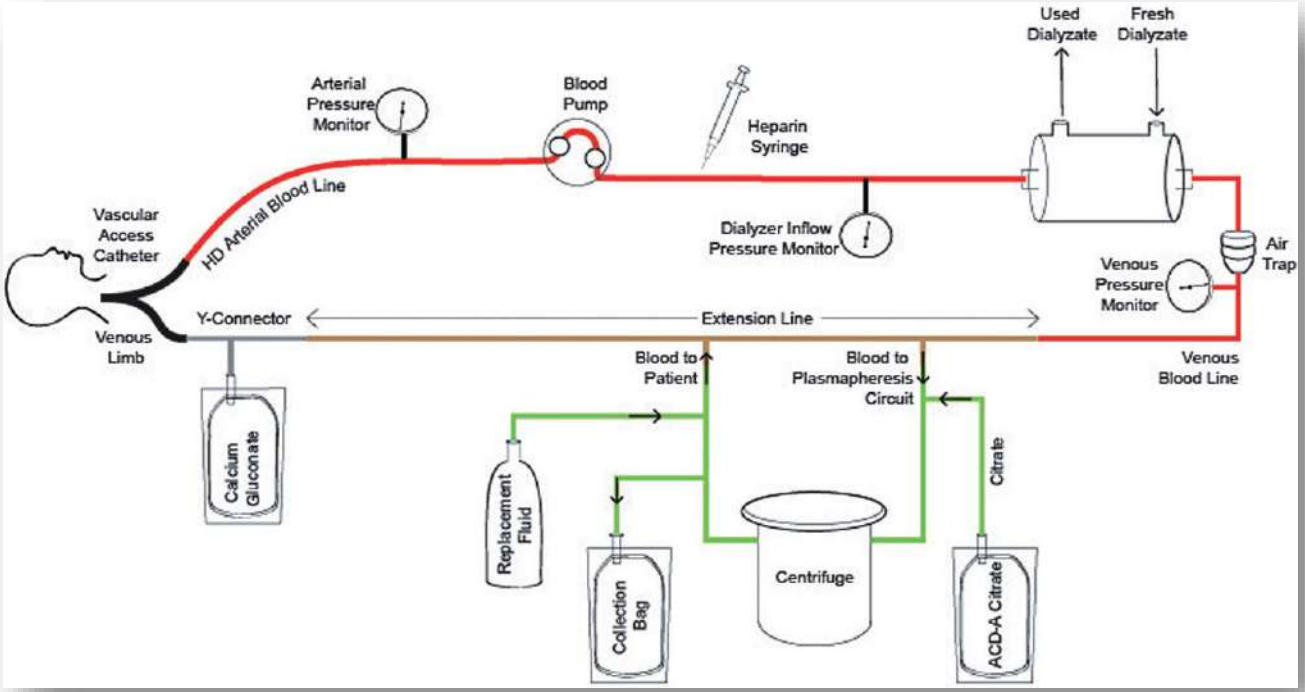
Parallel execution: antibody removal + metabolic control

Coordination between nephrology, transfusion medicine, and dialysis teams



Tandem TPE-HD: *Padova*

Tandem TPE-HD: *Padova*



Farah et al, Hemodial Int 2013

Wo Tandem TPE-HD: *Padova*

Lunedì	Martedì	Mercoledì	Giovedì	Venerdì	Sabato	Domenica
29	30	31	1	2	3	4
5	6	7	8	9	10	11
12 HD	13 TPE	14 HD	15 TPE	16 HD	17 TPE	18
19 TPE	20 HD	21 TPE	22 HD	23 TPE	24 HD	25 TPE
26 TPE HD	27 ✕	28	1	2	3	4
5	6	7	8	9	10	11

Tandem TPE-HD: *Padova*

Advantages:

Reduction of overall treatment time (patients-apheresis/dialysis staff)

Improvement of patient's QoL

Immediate correction of fluid, electrolyte & acid base balance

Reduction of citrate toxicity

Lunedì	Martedì	Mercoledì	Giovedì	Venerdì	Sabato	Domenica
29	30	31	1	2	3	4
5	6	7	8	9	10	11
12 HD	13 TPE	14 HD	15 TPE	16 HD	17 TPE	18
19 HD/TPE	20	21 HD/TPE	22	23 HD/TPE	24	25 TPE
26 HD/TPE	27	28	1	2	3	4
5	6	7	8	9	10	11

Take home messages

ABOi KT is feasible and safe with targeted and tailored apheresis strategies

Optia + Glycosorb® for higher titres

Tandem apheresis–dialysis enhances patient experience and treatment efficiency

Multidisciplinary Collaboration is crucial for optimal workflow and outcomes

REGIONE DEL VENETO
Azienda Ospedale Università Padova

Department of Transfusion Medicine

Director Alessandro Lanti

Therapeutic Apheresis Unit

Francesca Pavanello
Anca Irina Leahu
Claudia Santarossa
Massimiliano Barbieri
Ivano Bettella
Monica Chinchio
Monica Libero
Alessandra Masin
Adriano Visione

Immunohematology Lab

Paola Bagatella
Federica Spolaore
Tiziana Tison
and all the technicians

Kidney and Pancreas Transplantation Unit

Director Lucrezia Furian

Cristina Silvestre
Marianna Di Bello
Caterina Di Bella
Francesco Tuci

and all the nurses

Nephrology, Dialysis and Transplantation Unit

Director Federico Nalesso

Leda Cattarin
Marianna Alessi

and all the nurses & dialysis technicians

thank you