In the name of GOD

Therapeutic Apheresis in Renal Transplantation

Hassan Argani, Emeritus Professor of Nephrology

Principles & Mechanism

Various types of Apheresis

Strategy and technical issues

Indications in renal transplant

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Various types of Apheresis

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Indications in renal transplant

The ideal characteristics of removable substances by TA should have

- ❑Large molecular weight (>15 KDa)
- ❑Prolonged half-life ➔ Rapid elimination from the plasma is mandatory
- ❑Higher-percentage intravascular distribution
- ❑Low turnover rate

Distribution and Metabolism of Plasma proteins

Protein	Plasma Concentration, mg/mL	Mass, kDa	Intravascular, %	Fractional Turnover, %/d	Half-Life, d
IgA	2.6	160	42	25	6
IgD	0.02	175	75	37	2.8
IgE	0.0001	190	41	94	2.5
IgG	12.1	150	45	6.7	22
IgM	0.9	950	78	19	5
Albumin	42	65	40	10	17
Fibrinogen	2-4	340	80	25	4.2
C3	1.5	240	63	56	2

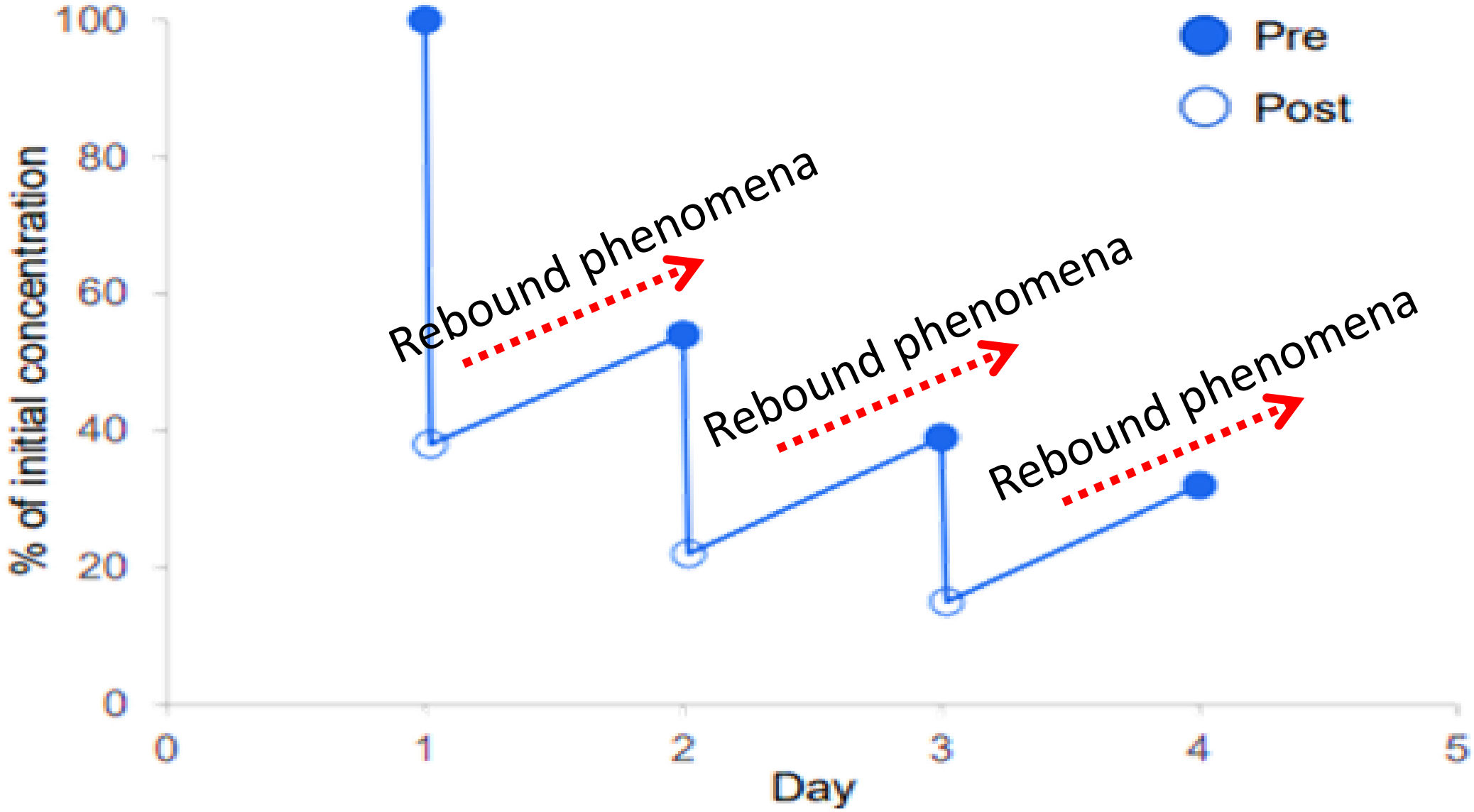
IgM – Approximately 75 percent of IgM is intravascular➔ As a result, only one or two procedures are usually required to rapidly reduce IgM levels.

IgG – Only 45 percent of IgG is intravascular, and within 48 hours, plasma IgG returns to approximately 60 percent of the pre-apheresis level➔ Consequently, a more rigorous regimen involving 5 procedures and immunosuppressive therapy are important to significantly reduce IgG levels

IgG removal in ABMR

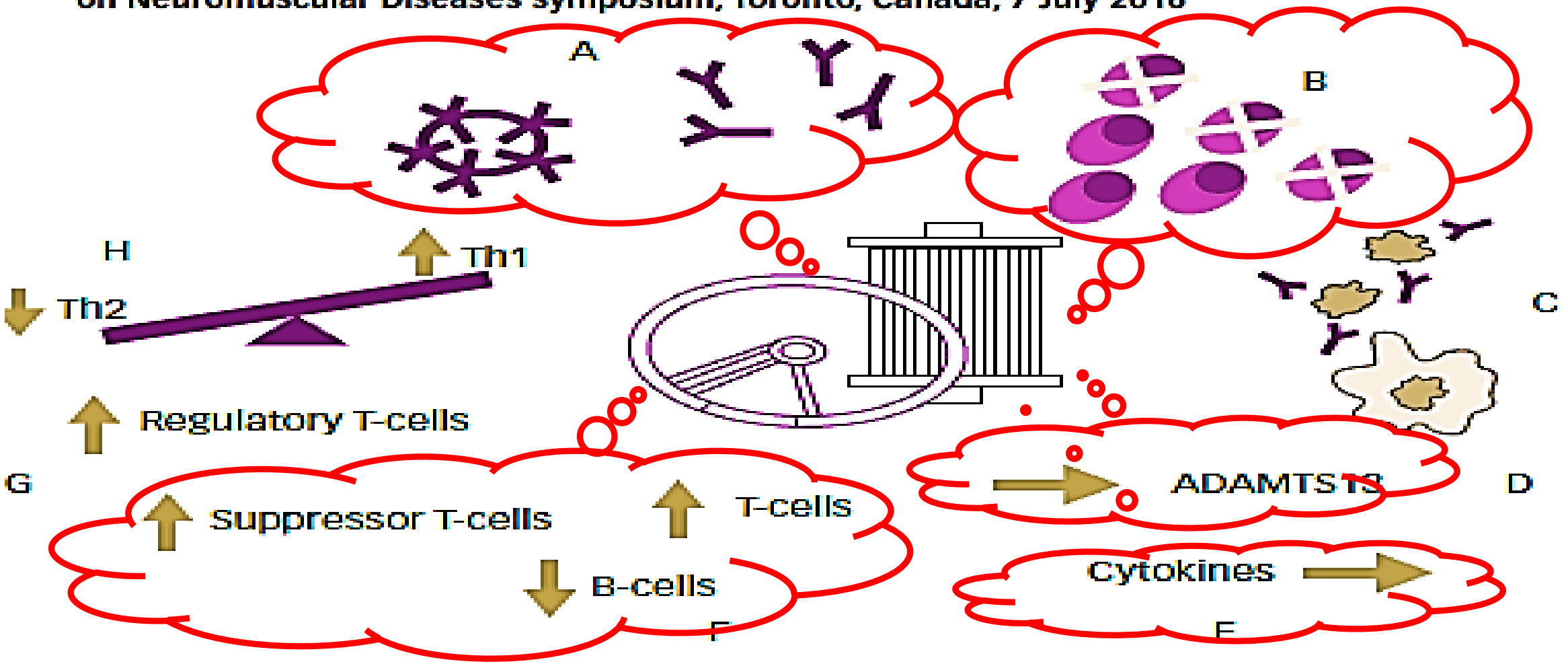
- As the IgG half life is 22 days even if immunosuppressive therapy could immediately inhibit new antibody production, the plasma concentration would decrease by only approximately 50 percent within 21 days. Such a delay is not acceptable in ABMR.
- Another benefit of TA is unloading of the reticuloendothelial system, which can enhance endogenous removal of circulating toxins.
- TA predisposes the lymphocyte clones to cytotoxic therapy.

IgG removal from 1 plasma volume exchanged per day for 3 days



The Immunomodulatory Role of Therapeutic Plasma Exchange in Peripheral Nervous System and Neuromuscular Diseases

Proceedings of a satellite symposium held at the 14th International Congress on Neuromuscular Diseases symposium, Toronto, Canada, 7 July 2016



Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Review

Reflections on the usefulness of extracorporeal photopheresis in renal transplant rejection: A concise review of the involved mechanisms and therapeutic perspectives

Earlier TA in the course of acute rejection has better results

Characteristics of Common Drugs Removed by TAP

Drug	Protein Binding, %	Volume of Distribution, L/kg
Acetaminophen	<3	0.1
Acetylsalicylic acid[a]	80-90	0.1-0.2
Azathioprine	30	0.6
Cefazolin[a]	80	0.13-0.22
Ceftriaxone[a]	90	0.12-0.18
Cyclosporine	90-98	13
Cyclophosphamide	23	0.8
Digoxin	20-30	5-8
Eculizumab	NA	5-8
Glyburide[a]	99	0.16-0.3
Heparin[a]	>90	0.06-0.1
Ibuprofen[a]	99	0.15-0.17
Levothyroxine[a]	90	0.1-0.2
Prednisone-prednisolone	90-95	0.6-0.7
Rituximab	NA	3.1-4.5
Valproic acid[a]	90	0.19-0.23
Tobramycin	10	0.25
Vancomycin	70	0.39
Verapamil[a]	90	NA
Warfarin[a]	97-99	0.11-0.15

Drug Removal by TA

- Plasma exchange may affect drug concentrations through direct removal or via removal of metabolizing enzymes.
- TPE removes only 1% of prednisolone, and additional doses are not required after TPE.
- Cyclosporine and tacrolimus are predominantly intracellular and not affected by plasma exchange.
- Rituximab may be removed up to 50%, so a dose can be administered after TPE session.

Principles & Mechanism

Various types of Apheresis

Strategy and technical issues

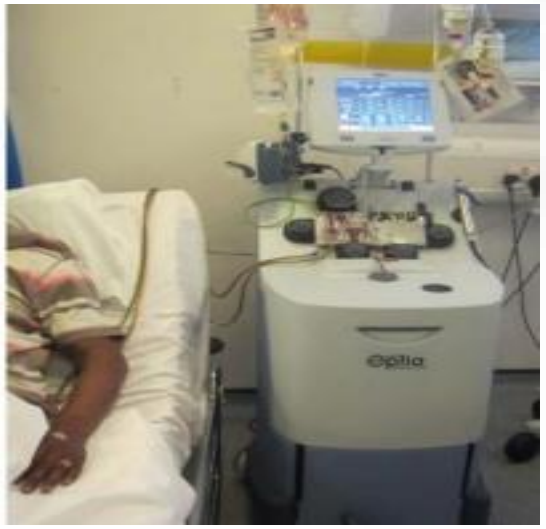
Indications in renal transplant

Apheresis modalities

Procedure	Target Molecule
Adsorptive cytapheresis	Monocytes, granulocytes
ß$_2$-microglobulin column	ß$_2$-microglobulin
Double filtration plasmapheresis	Autoantibodies, immune complexes, lipoproteins
Erythrocytapheresis	Red blood cells
Extracorporeal photopheresis	Buffy coat (white blood cells and platelets)
Immunoadsorption	Immunoglobulins
Leukocytapheresis	White blood cells
Lipoprotein apheresis	Lipoprotein particles
Red blood cell exchange	Red blood cells (exchanged for replacement fluid)
Rheopheresis	High-molecular-weight plasma components (fibrinogen, α_2-macro-globulin, low-density lipoprotein cholesterol, and IgM)
Therapeutic plasma exchange	Plasma (exchanged for replacement fluid)
Thrombocytapheresis	Platelets

AJKD Vol 81 | Iss 4 | April 2023; 475-492

TPE: Comparison of centrifugation and membrane separation therapeutic PP



Centrifugation TPE

Calcium

Anticoagulation
Citrate

Centrifuge

Discarded
Patient's
plasma

Replacement fluid
Donor plasma/Albumin

Because lower blood flow rates are sufficient, peripheral vein access will be ok.

Membrane TPE

Anticoagulation
Heparin

Blood pump

Replacement fluid
Donor plasma/Albumin

Plasma
separation
filter

Discarded
Patient's
plasma

Blood pump

Calcium

Table 2. Apheresis Versus Hemodialysis

Characteristic	Therapeutic Plasma Exchange		Hemodialysis
	Centrifugation	Membrane Filtration	
Mechanism	Centrifugal force	Convection	Diffusion and/or convection
Blood flow, mL/min	10-150	150-200	Continuous: 100-300; intermittent: 200->400
Blood volume in circuit, mL	180	125	160-280
Plasma extraction, %	80	30	NA
Molecular weight cutoff, Da	>15,000	>15,000	<15,000
Vd, L/kg	Low (<0.3)	Low (<0.3)	Moderate (≤1.5-2)
Protein binding, %	>80	>80	<80
Anticoagulation	Citrate	Heparin	Heparin
Sterilization	γ-Irradiation; ethylene oxide	γ-Irradiation; ethylene oxide	Ethylene oxide; steam; electron beam; γ-irradiation

May be used *without* AVF or CV Catheter

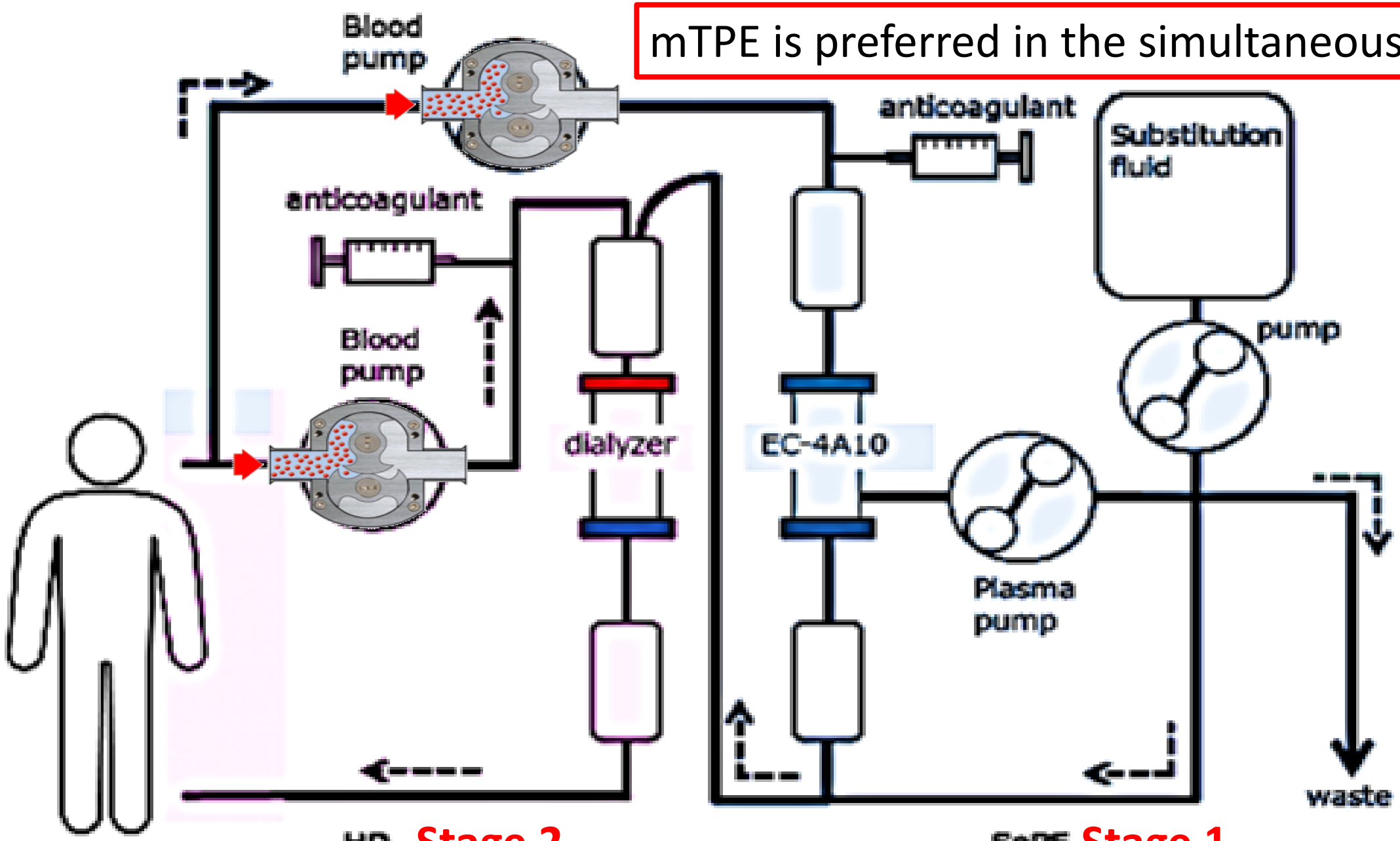
Is more effective for removing of higher molecular weights such as IgM and immune complexes

Simultaneous TAP with HD

- In patients on the hemodialysis for kidney failure, alkalemia may result from repeated apheresis treatments when FFP is the primary replacement fluid. Therefore, if TPE and dialysis are required on the same day, *TPE should be performed first* to allow subsequent dialysis to correct the blood pH or hypervolemia resulting from TPE.
- Importantly, *TPE should not be used as an ultrafiltration* procedure by intentionally replacing less than the exchanged volume

Simultaneous TA with HD

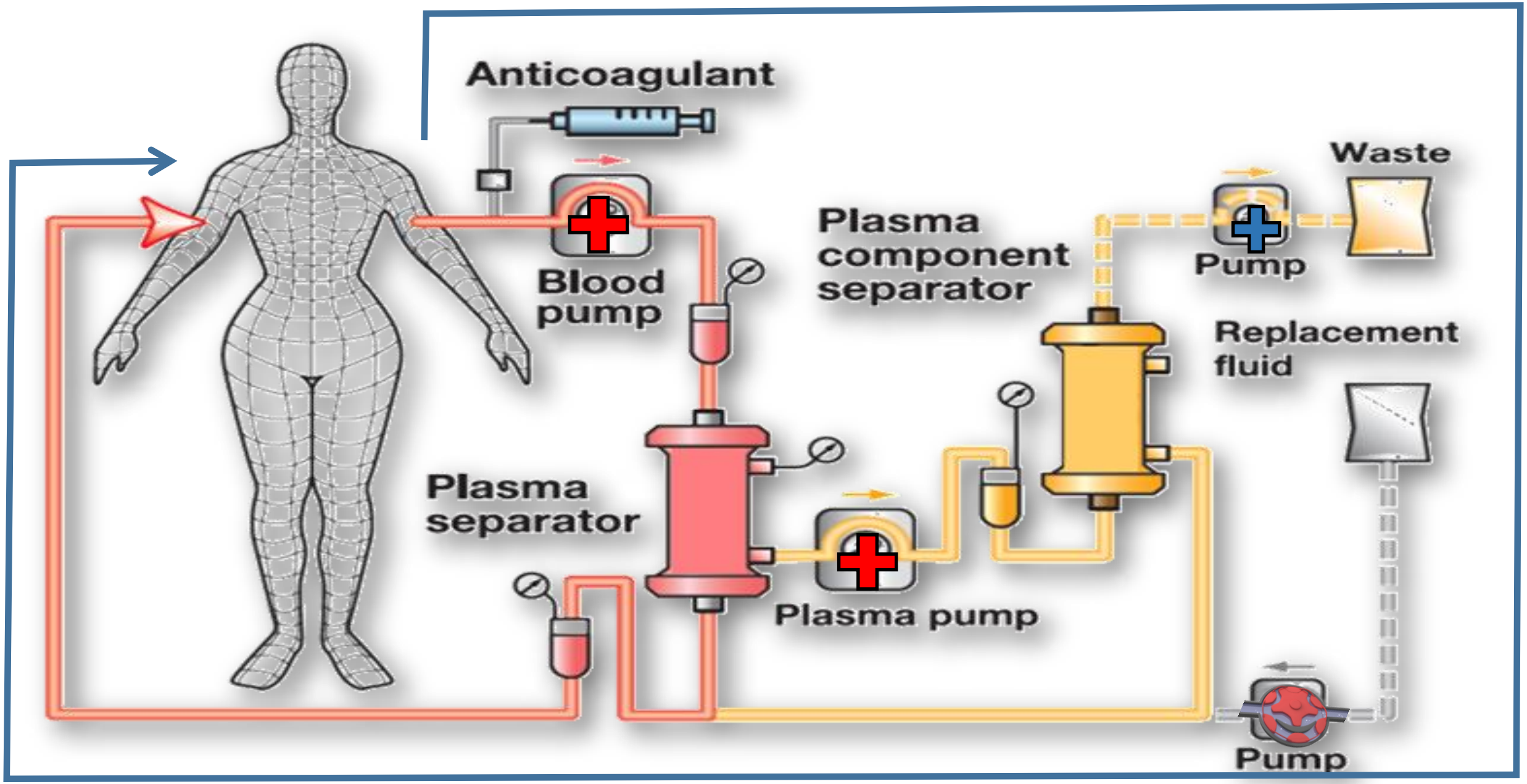
mTPE is preferred in the simultaneous cases



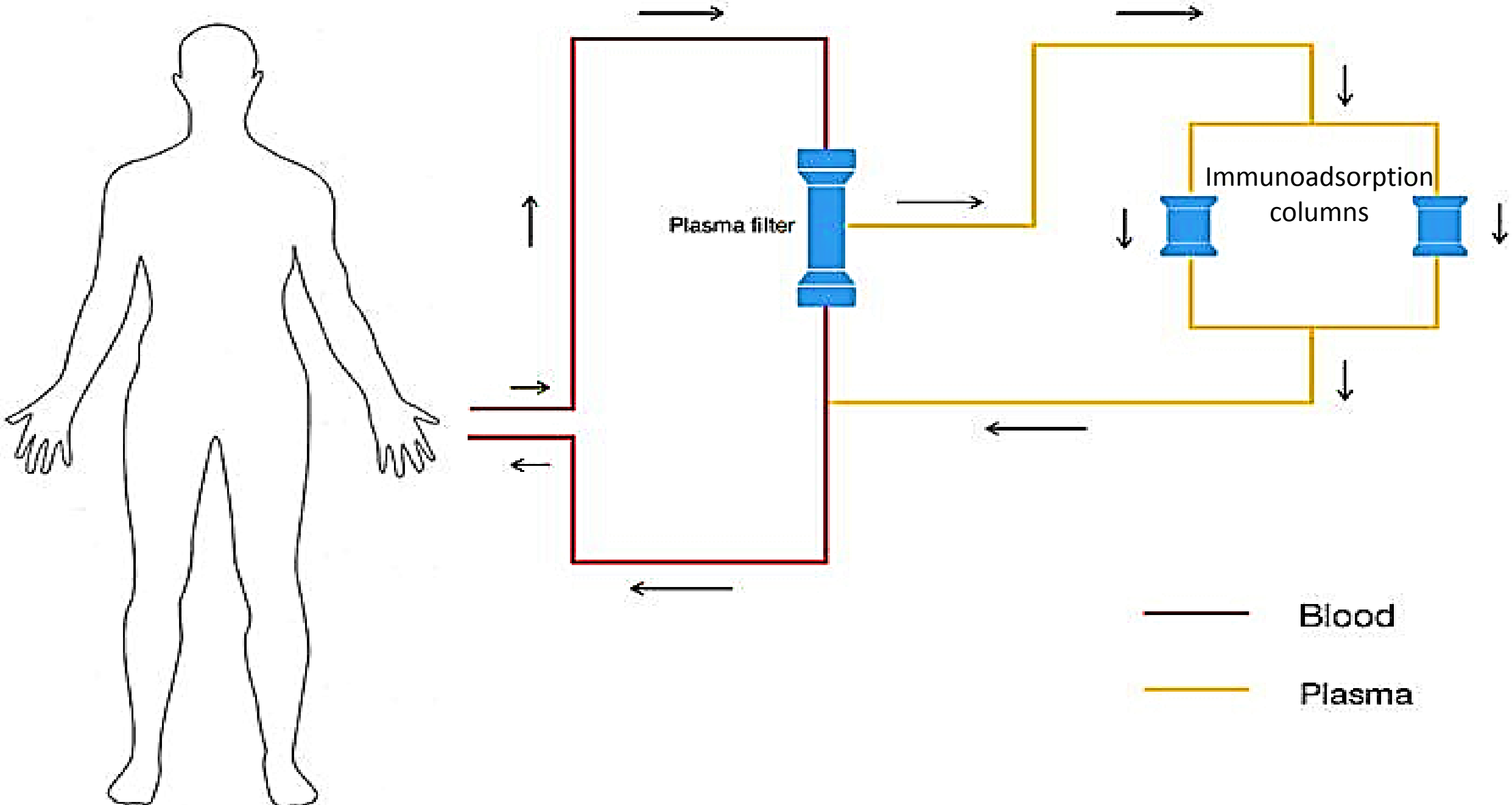
Selective TA techniques

- Double filtration plasmapheresis
- Immunoadsorption

Schematic presentation of DFPP



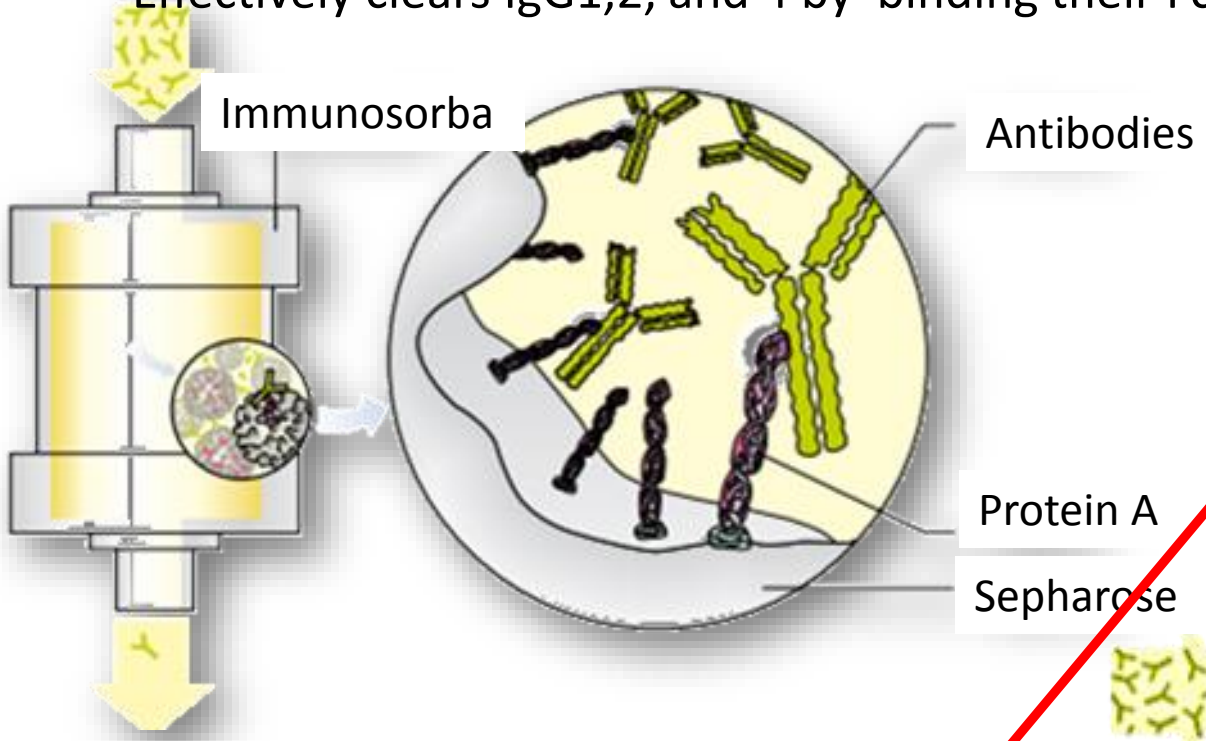
Immunoadsorption

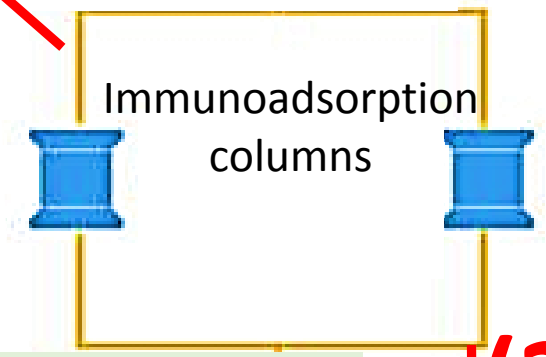


Immunoadsorption

IA using immobilized staphylococcal protein A

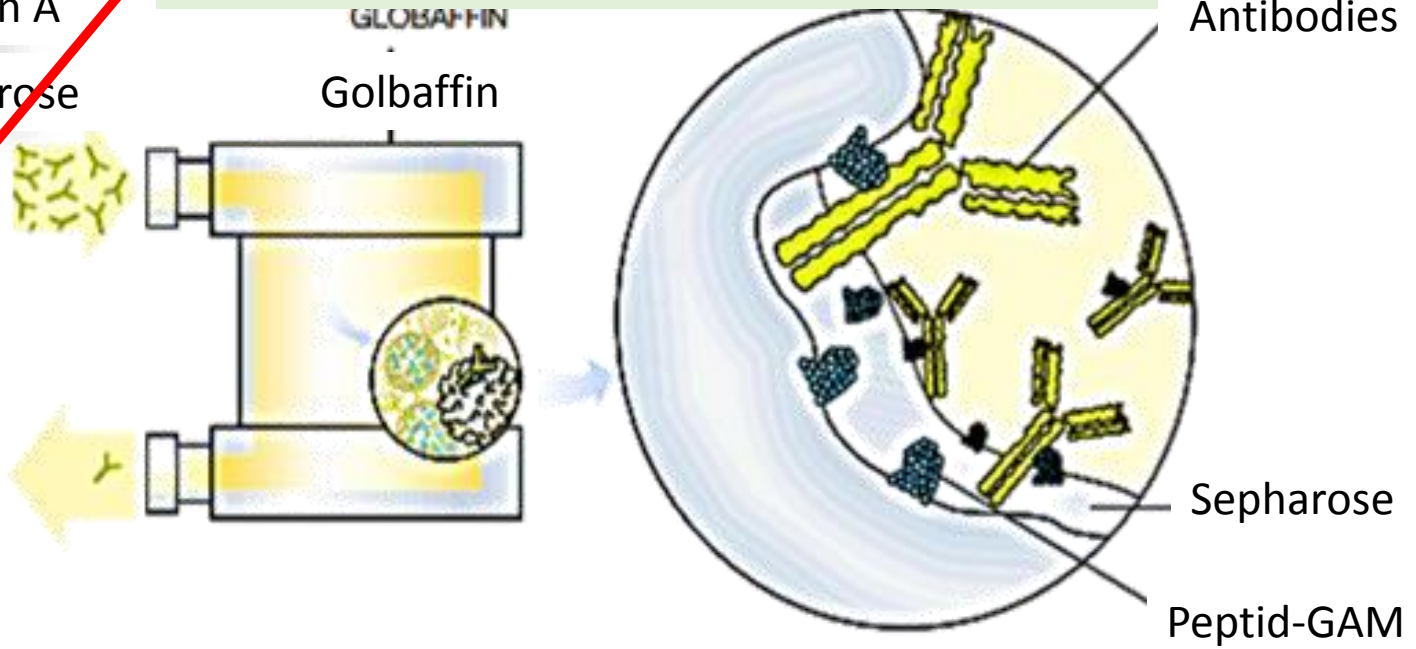
Effectively clears IgG1,2, and 4 by binding their Fc portions





IA using immobilized antibodies

(2)



IA using immobilized antigens and synthetic epitopes

It is s the most specific IA

Immunoadsorption Vs. plasmapheresis

- **IA** → better tolerability
- **IA** → lower likelihood of allergic reactions
- **IA** →can treat larger plasma volumes with higher antibody removal
- **IA** →has much more price

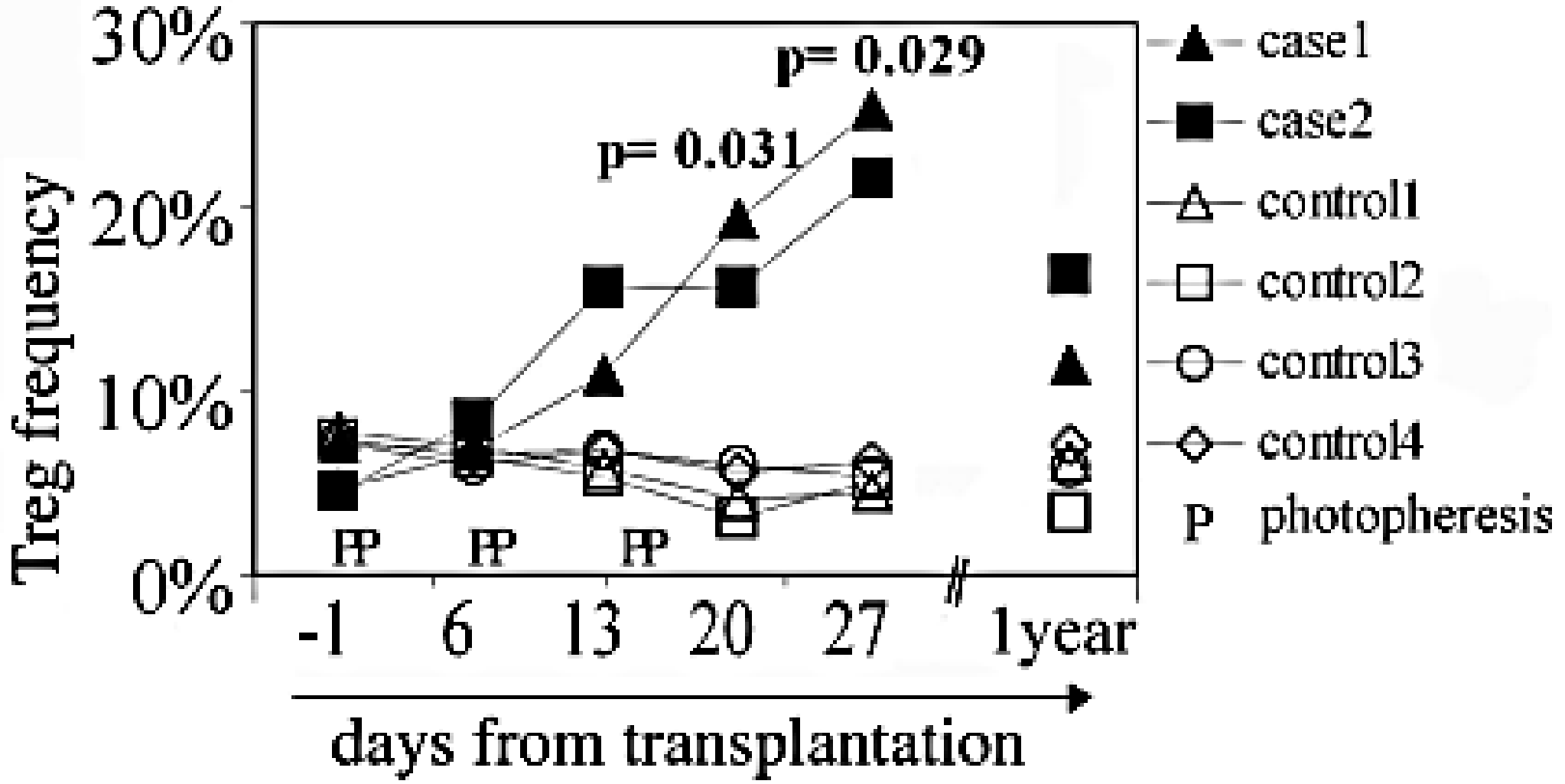
Induction of Regulatory T Cells After Prophylactic Treatment With Photopheresis in Renal Transplant Recipients

Andrea Lamioni,[1] Rita Carsetti,[1] Antonia Legato,[2] Attilio Landolfo,[3] Giancarlo Isacchi,[3,4] Francesco Emma,[2] Gian Franco Bottazzo,[5] and Luca Dello Strologo[2,6]

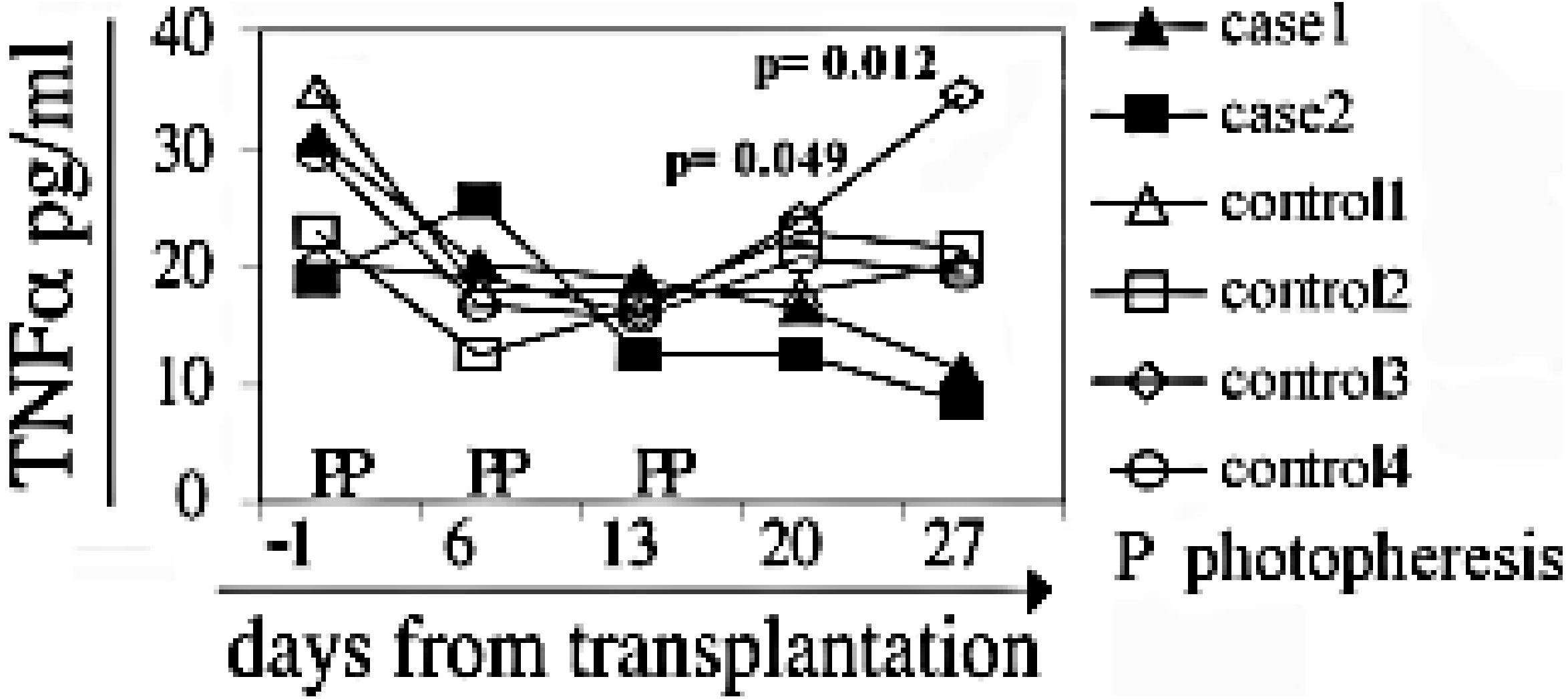
Extracorporeal photopheresis (ECP), originally used to treat cutaneous T-cell lymphoma, also has been applied to the therapy of transplant rejection. Our aim was to investigate the biologic response in two children who underwent kidney transplantation with ECP as prophylactic treatment. They received conventional immunosuppressive therapy and ECP immediately after transplantation: six applications over the course of 3 weeks. During a 12-month follow-up, the clinical course was favorable in both patients; renal histology was normal 6 months after transplantation. When compared with four transplanted controls, the ECP-treated patients showed lower tumor necrosis factor-α serum levels in the short-term and a marked increase of Foxp3-positive T-regulatory cells. T-regulatory cells were still higher than in the controls 1 year after transplantation. These preliminary results suggest that the addition of ECP to standard immunosuppressive therapy induces a tolerogenic shift in the immune system of kidney transplanted patients and may pave the way to preventing chronic rejection.

Keywords: Photopheresis, Regulatory T cells, Kidney transplantation, Children.

(*Transplantation* 2007;83: 1393–1396)



Transplantation 2007;83: 1393–1396



Transplantation 2007;83: 1393–1396

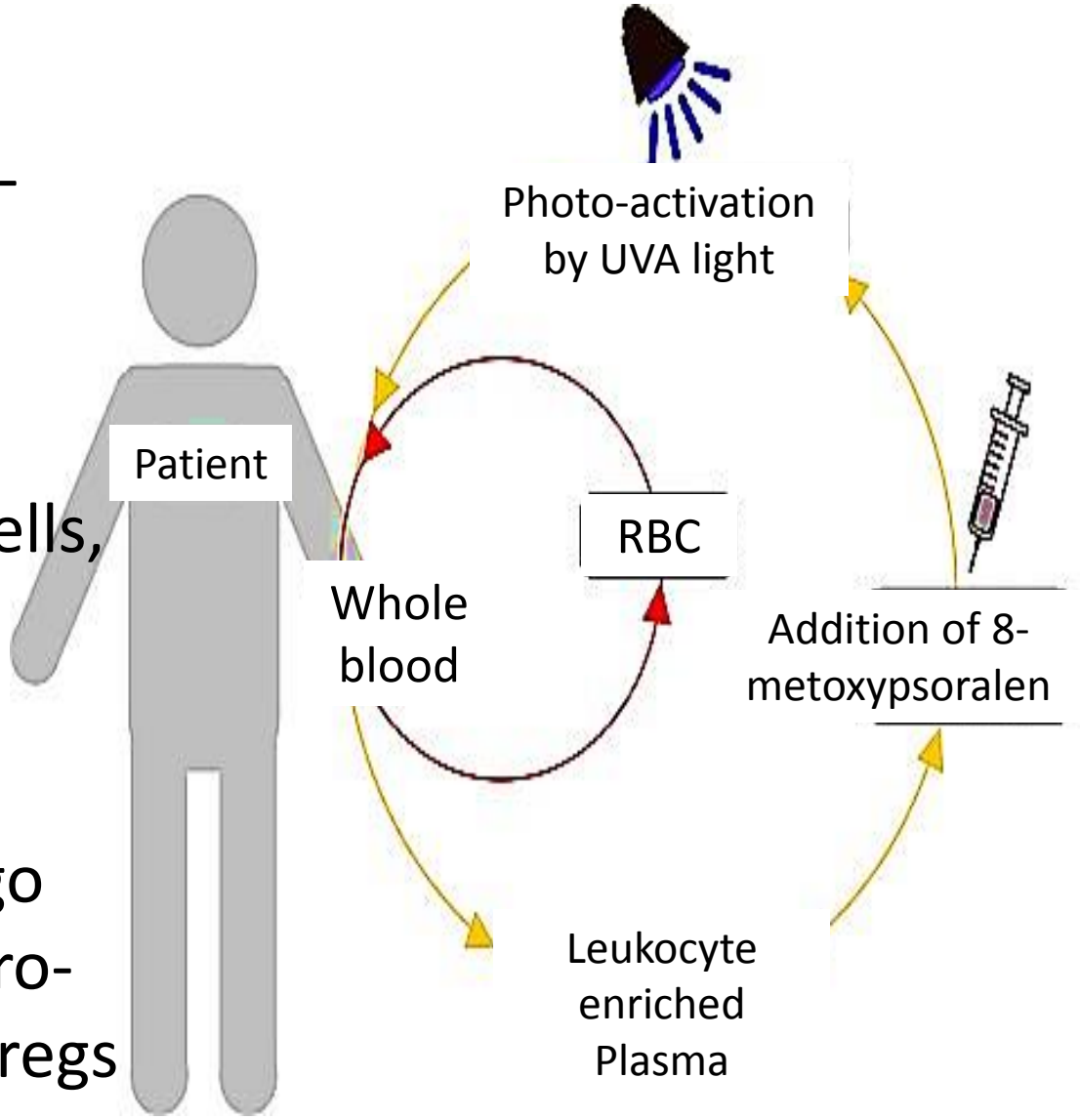
Conclusion

- ECP treatment enhances the level of Treg cells and show that this increase persists for up to 1 year without the need for a recall ECP.

Transplantation 2007;83: 1393–1396

Extracorporeal photopheresis

- It begins with the separation of WBCs from plasma by centrifugation➔ Then the WBC undergoes extracorporeal treatment with 8-methoxypsoralen (8-MOP) and exposure to ultraviolet A.
- 8-MOP+ UVA➔ Crosslinking of pyrimidine bases in DNA➔ To apoptosis of lymphoid cells, largely T-cells.
- Reinfusion of the phagocytosis of apoptotic lymphoid cells is performed by immature dendritic antigen-presenting cells➔ undergo maturation and present self-antigens in a pro-tolerant signaling environment➔ Induces Tregs



Successful Treatment of Recurrent Rejection in Renal Transplant Patients with Photopheresis

ROBERTO DALL'AMICO, LUISA MURER, GIOVANNI MONTINI, BARBARA ANDREETTA, GIOVANNI-FRANCO ZANON, GRAZIELLA ZACCHELLO, and FRANCO ZACCHELLO

Department of Pediatrics, University of Padua, Padova, Italy.

J Am Soc Nephrol 9: 121-127, 1998

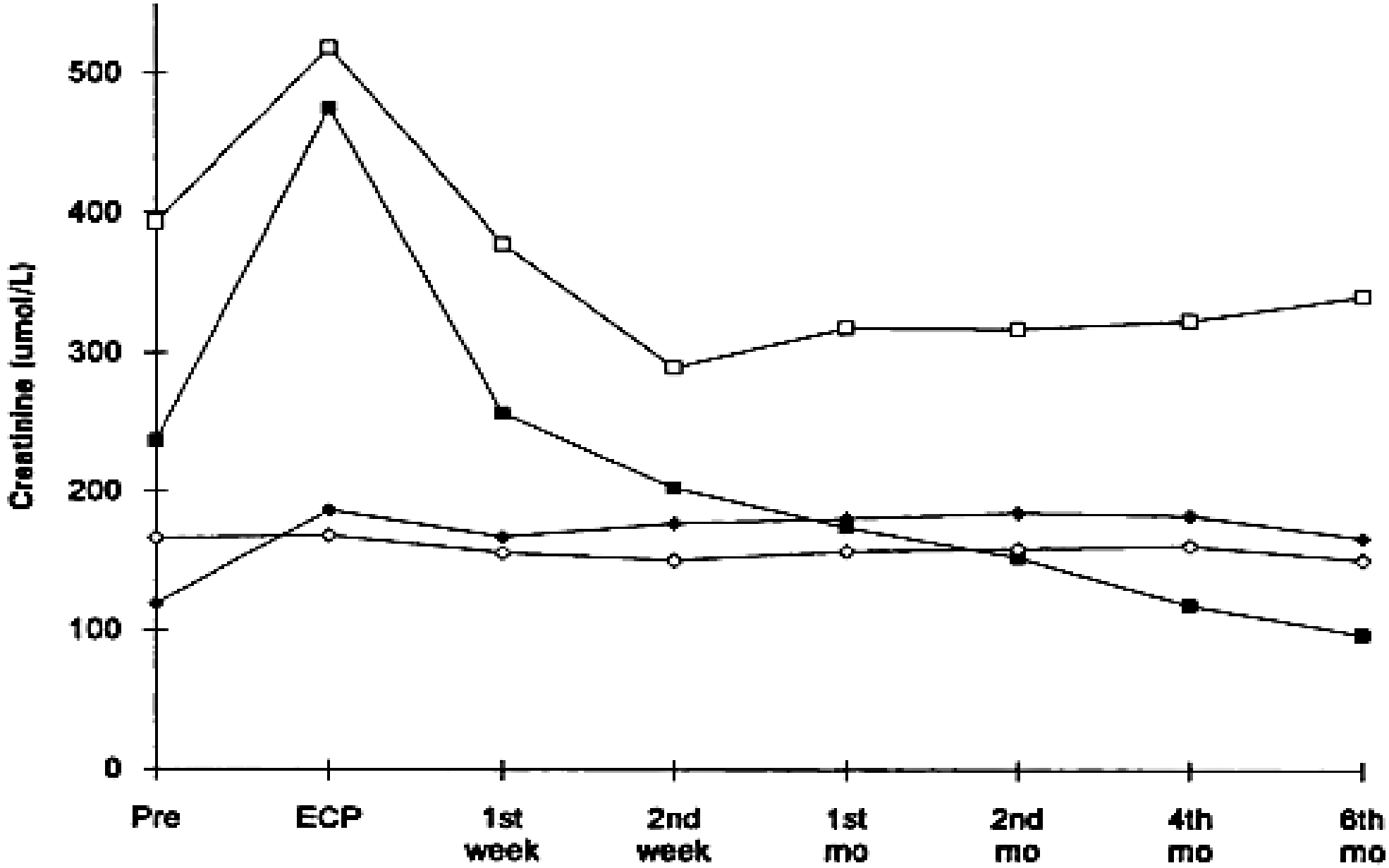


Figure 1. Serial values of serum creatinine during treatment with photopheresis (ECP).

J Am Soc Nephrol 9: 121-127, 1998

The advantage of ECP

- ECP is an effective and safe therapy for renal transplant patients while recurrent rejection episodes not responsive to standard immunosuppression.
- In addition to the standard immunosuppressive action of ECP, It does not increase the risk of infection or malignancy.
- ECP can be used as a part of calcineurin inhibitor sparing protocols to reduce drug side effects such as CNI nephrotoxicity.

ELSEVIER

Application of Extracorporeal Photopheresis in Kidney Transplant Recipients: Technical Considerations and Procedure Tolerance

M. Kusztal, R. Kłak, M. Krajewska, M. Boratyńska, D. Patrzałek, and M. Klinger

- Two consecutive days every week during the first month (8 procedures) were then tapered to 2 every other week (4–8 procedures). The total number of ECP sessions varied from 12 to 16.
- Each session lasted 2–3 hours.
- Standard heparin solution was used for anticoagulation.
- All subjects were asked to wear sunglasses and use skin sun-protectors for 15 for 24 hours after the ECP session to avoid phototoxic skin reactions.

Transplantation Proceedings, 43, 2941–2942 (2011)

ESOT | Transplant International

ORIGINAL RESEARCH
published: 12 January 2023
doi: 10.3389/ti.2023.10840

Check for updates

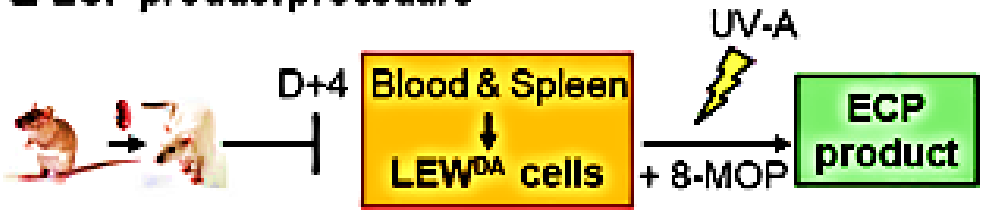
Extracorporeal Photopheresis Improves Graft Survival in a Full-Mismatch Rat Model of Kidney Transplantation

Extracorporeal photopheresis improves graft survival in a full-mismatch rat model of kidney transplantation

Background. Extracorporeal photopheresis (ECP) is an immunomodulatory therapy based on the infusion of autologous cellular products exposed to ultraviolet light in the presence of a photosensitizer.

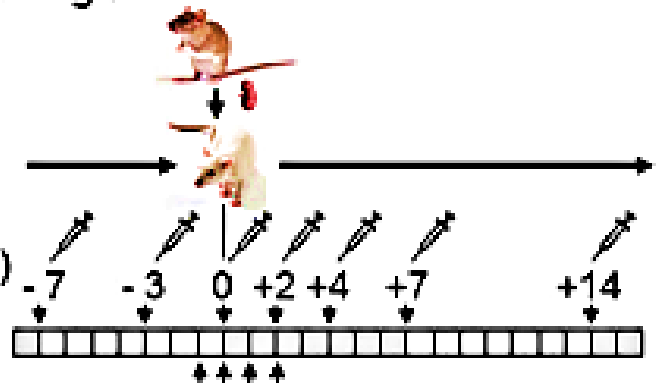
Methods

❑ ECP product procedure



❑ Experimental design

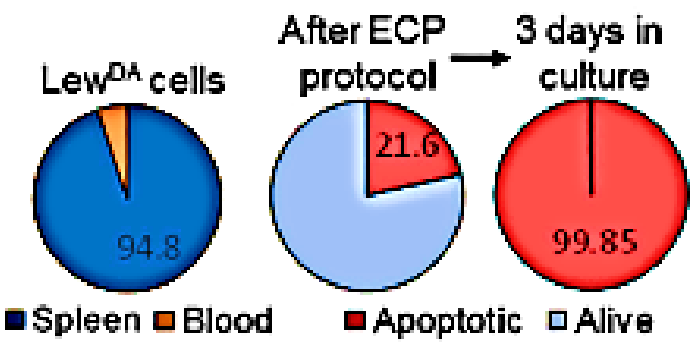
➢ **Study groups**
- Ø cells
- Lew^{DA} cells
- ECP (low dose)
- ECP (high dose)



TAC$_{im}$(0.25mg/Kg/day)

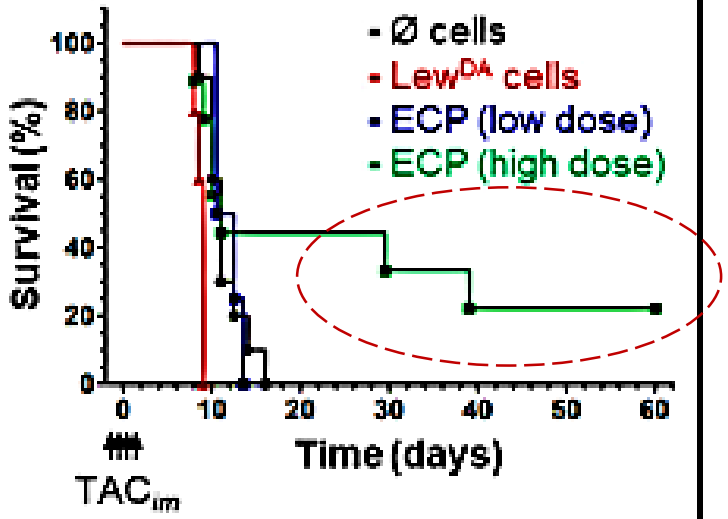
Results

❑ ECP product characteristics



ECP product is constituted mainly by splenocytes without proliferative capacity and drive to apoptosis.

❑ Impact of ECP therapy on rat survival



Conclusion. ECP treatment increases kidney graft survival in full-mismatch rat model of acute rejection and is a suitable immunomodulatory therapy to be explored in kidney transplantation.

Piñeiro G.J., et al. *Transpl. Int.* 2023

doi: 10.3389/ti.2023.10840

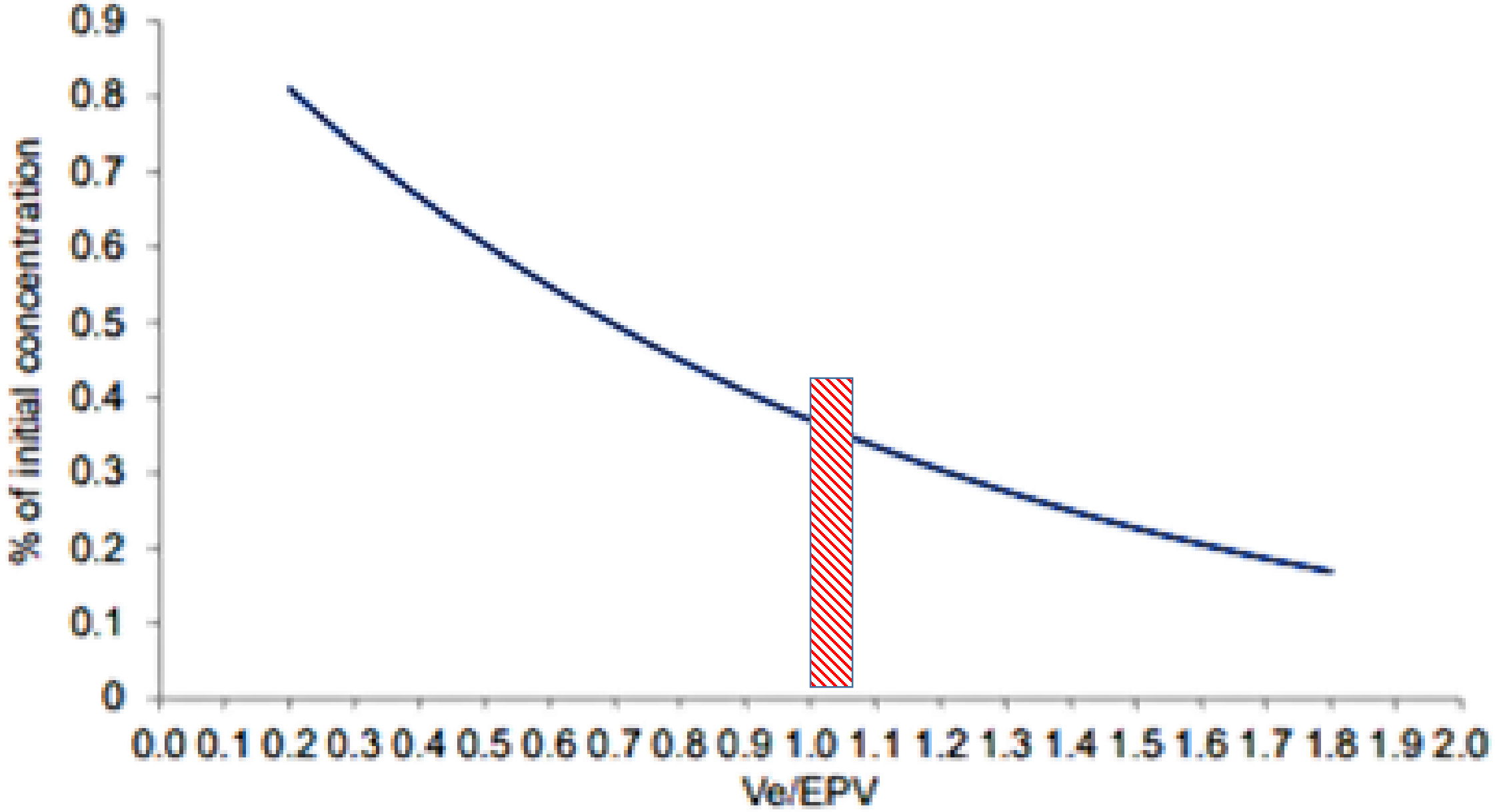
Principles & Mechanism

Various Types of Apheresis

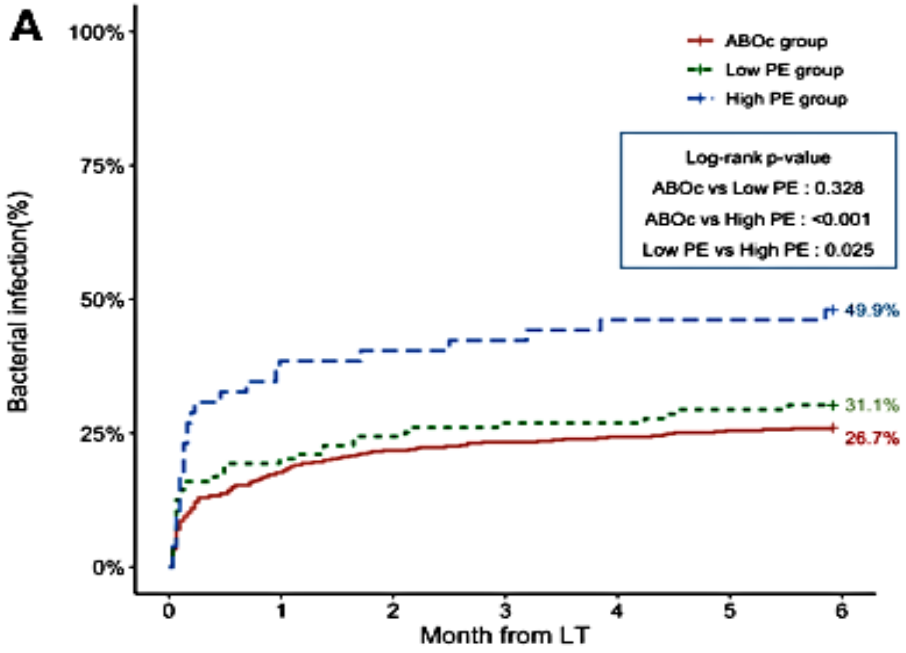
Strategy and technical issues

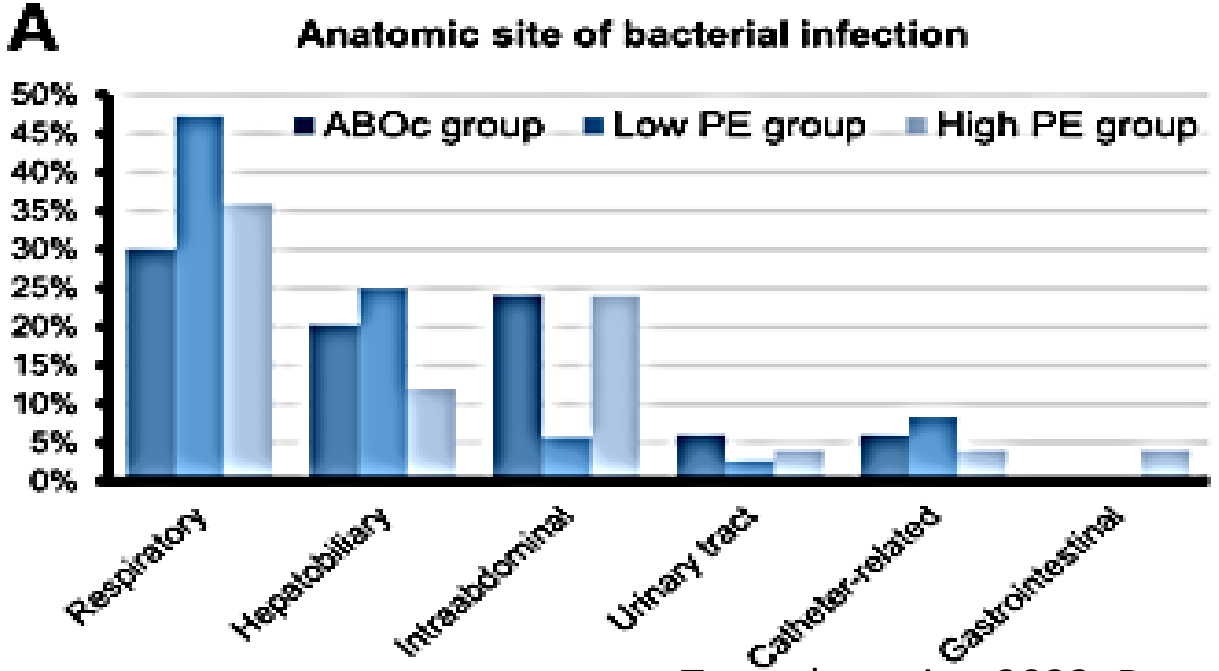
Indications in renal transplant

The relationship of percentage decrease in initial concentration of substances as a function of volume exchanged (Ve) relative to estimated plasma volume (EPV).



High Number of Plasma Exchanges Increases the Risk of Bacterial Infection in ABO-incompatible Living Donor Liver Transplantation





Transplantation 2023; December; 1-9

Kaplan's equation

Estimated plasma volume (in liters) =
0.07 x weight (kg) x (1 - hematocrit)

Choice of replacement solution

Solution	Advantage	Disadvantage
Albumin	• No risk of hepatitis • Allergic reactions rare • No concern about ABO blood group	• Expensive • No coagulation factors • No immunoglobulins
Fresh frozen plasma	• Coagulation factors • Immunoglobulins • “Beneficial” factors complement	• Risk of hepatitis • Allergic reactions • Must be ABO compatible • Citrate loaad

Albumin 5% not 20%!

Albumin concentration	Typical usages & benefits	drawbacks
20%	Hypovolemic Shock, Oncotic deficiency, paracentesis in cirrhotic ascit, ARDS, Severe NS, Severe Burn, Cardiopulmonary bypass, Hypotension during HD	Edema and fluid overload, Hypersensitivity reactions, Cost
5%	❖ Volume loss, Plasmapheresis. ❖ markedly lowered risks of pathogen transmission and anaphylactic reactions	post-apheresis dilution coagulopathy, and a net loss of immunoglobulins

Albumin

- Commercially available 5% albumin solutions contain approximately 145 mmol/L sodium and <2 mmol/L potassium.
- TPE followed by albumin replacement will result in a 50%-60% reduction in anticoagulant factors.
- Coagulation testing should not be performed for 8- 12 hours after albumin replacement.
- If cost is a limitation, an 80:20 albumin–saline solution combination can be used, with a minimum ratio of 70:30 → 4-5 vials of 20% of Albumin+1.2 liter of NS is enough.
- These diluted replacement fluids carry a higher risk for hypotension.
- It has a lower risk than plasma of hypersensitivity reactions, transfusion-related acute lung injury, and transmission of infection.

Frozen Plasma

- Plasma is primarily used to replenish ADAMTS13 in TTP and clotting factors in patients with bleeding
- FFP contains approximately 7 mmol citrate per unit, increasing the risk for citrate toxicity with large-volume infusions.
- Because unit size is 200-300 mL, a single plasma volume exchange of 2.5 L will require 10 U obtained from many donors.
- If there is a history of hypersensitivity to FFP, pre-treatment with steroids, diphenhydramine, and ephedrine is recommended.
- Risks associated with donor plasma include transfusion reactions and citrate toxicity.

Research Article

Indian J Crit Care Med 2017;21:857-60

Plasmapheresis: A Retrospective Audit of Procedures from a Tertiary Care Center in Southern India

O. T. Ahammed Nizar, Pratheeksha Rai, Shobhana Nayak Rao[1], M. Pradeep Shenoy[1]

Departments of Internal Medicine and [1]Nephrology, K.S. Hegde Medical Academy, Mangalore, Karnataka, India

As replacement fluid, it has been used a protocol of 100 ml of 20% albumin diluted in 1 L of normal saline along with 2–3 units of FFP.

=1500cc

The prices of TAP procedures

- Each session of IA: 900-1000 €
- Plasmapheresis: $50,000 or more per protocol
- disposables costing between $1,500 per patient/session in the US, £880 in the UK, and 800 Euros in the Germany

European Society for Organ Transplantation 25 (2012) 506–517

List of diseases that DFPP is National Health Insurance covered as of April 2020.

Neurological Disorders	Myasthenia gravis (MG)
	Guillain-Barré syndrome (GBS)
	Chronic inflammatory demyelinating polyneuropathy (CIDP)
	Multiple sclerosis (MS)
Rheumatic Disorders	Systemic lupus erythematosus (SLE)
	Malignant rheumatoid arthritis (MRA)
	Kawasaki disease
Metabolic Disorders	Familial hypercholesterolemia (FH)
Organ Transplantations	ABO/HLA incompatible kidney transplant
	ABO/HLA incompatible liver transplant
Renal Disorders	Anti-glomerular basement membrane (GBM) antibody mediated rapidly progressive glomerulonephritis (RPGN)
	Anti-neutrophil cytoplasm autoantibody (ANCA) mediated RPGN
	Focal segmental glomerulosclerosis (FSGS)
Hematological Disorders	Thrombotic thrombocytopenic purpura (TTP)
	Hemolytic uremic syndrome (HUS)
	Multiple myeloma (MM)
	Macroglobulinemia
	Hemophilia with inhibitor
Hepatic Disorders	Chronic hepatitis C
	Acute hepatic failure
	Postoperative hepatic failure
Dermatologic Disorders	Pemphigus vulgaris
	Pemphigoid
	Toxic epidermal necrolysis (TEN)
	Stevens-Johnson syndrome
Others	Arteriosclerosis obliterans (ASO)
	Severe blood-type incompatible pregnancy

Laboratory tests should be undertaken before each PP session

Investigation	Action to Take
Platelet count	Use plasma exchange with caution if platelet count < 40 × 10^9/L unless disease itself associated with thrombocytopenia (e.g., aHUS/TTP), and use FFP as part of replacement fluid.
Plasma fibrinogen	<150 mg/dL, should use FFP as part of exchange fluid.
PT, PTT	If prolonged more than 2–3 seconds, use FFP as part of exchange fluids.
Serum Ca	If <2.1 mmol/L (<8.4 mg/dL), increase amount being provided with replacement albumin/FFP.
Serum K	Can be highly variable depending on changing kidney function in addition to plasma exchange treatment; adjust potassium replacement according to serum potassium.

Anticoagulation in the TPE

Heparin	Citrate
The choice anticoagulant In the mTPE	The choice anticoagulant in the cTPE
It needs 2 times more than HD, because ATIII is removed	Hypocalcemia more common
Trombocytopenia	

Complications Associated With TPE

Access related	**1%-20%**
Electrolyte disorders	**9%-19%**
Thrombocytopenia	**1%-5%**
Hypotension	**0.5-15%**
Coagulopathy	**<2%**

Principles & Mechanism

Various Apheresis

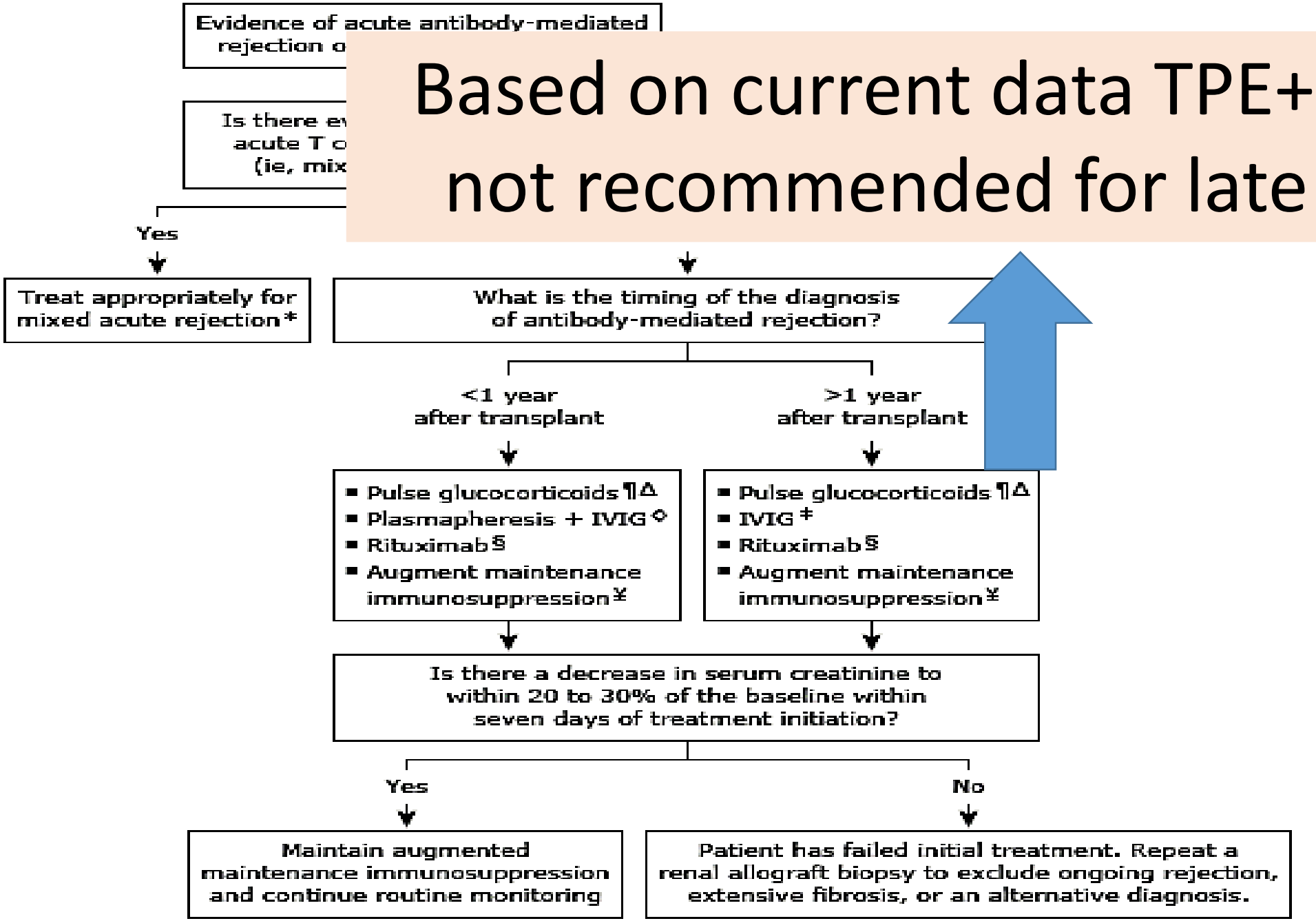
Strategy

Indications in renal transplant

Clinical indications for therapeutic apheresis in kidney transplantation

1. **ABMR**
2. **Recurrence of primary FSGS**
3. Desensitization protocols
4. Prevention and treatment of complement-mediated aHUS
5. De novo TMA
6. Antiphospholipid syndrome and systemic lupus erythematosus
7. Recurrent and de novo anti-GBM disease
8. Recurrence of ANCA- AAV

Based on current data TPE+ IVIG is not recommended for late AMR.



Uptodate 2023

The current management of ABMR based on the ASFA guideline

- TPE is important in the management of acute AMR after transplant.
- Management: AMR can be treated with TPE, DFPP,IA, always in conjunction with other immunosuppressive drugs;
- Following IA usually a rebound of antibodies is seen➔ Repeated post-transplant IA to avoid antibody rebound.
- TPE prescription:
  - Plasma volume: 1-1.5 EPV
  - Frequency: Daily or every other day
  - Replacement fluid: Albumin or FFP plus IVIG 100-200 mg/kg
  - Duration: TPE is usually daily or every other day for 5 or 6 sessions or based on clinical outcomes and decrease in donor-specific antibody Titers.

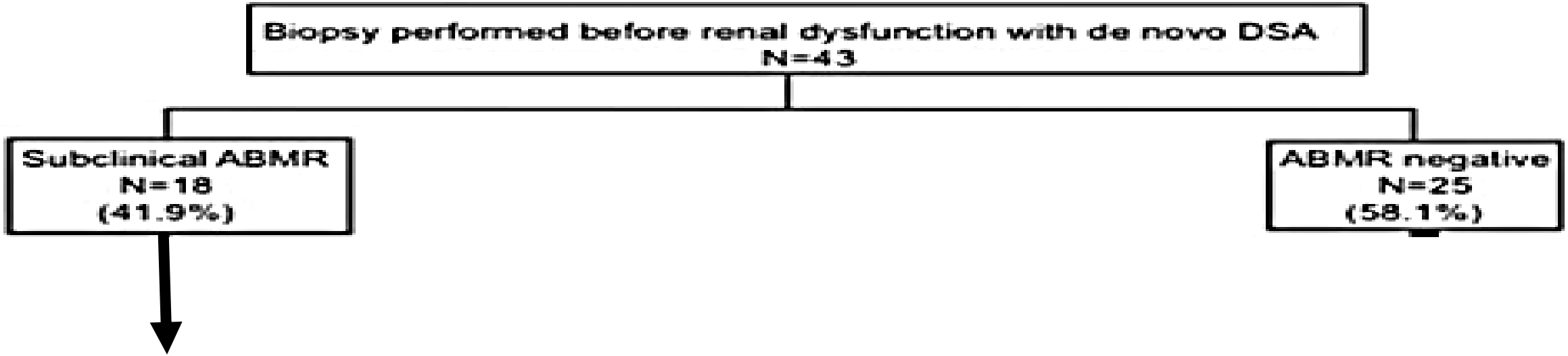
Original Clinical Science—General

De Novo Anti-HLA DSA Characteristics and Subclinical Antibody-Mediated Kidney Allograft Injury

Takayuki Yamamoto, MD, PhD,[1] Yoshihiko Watarai, MD, PhD,[1] Asami Takeda, MD, PhD,[2] Makoto Tsujita, MD,[1] Takahisa Hiramitsu, MD,[1] Norihiko Goto, MD, PhD,[1] Shunji Narumi, MD, PhD,[1] Akio Katayama, MD, PhD,[3] Kunio Morozumi, MD, PhD,[4] Kazuharu Uchida, MD, PhD,[5] and Takaaki Kobayashi, MD, PhD[5]

(Transplantation 2016;100: 2194–2202)

Treatment flow diagram



DFPP + Rituximab

Treatment effective rate was only 44%➔ Did not show any beneficial effect

(Transplantation 2016;100: 2194–2202)

Recurrent FSGS Following Kidney Transplant

- The etiology has been postulated for anti-nephrin antibodies and toxic lipoproteins
- The risks of recurrence of primary FSGS is generally 20%-50% in the first allograft and 80%-100% in subsequent allografts.
- Despite treatment, 30%-60% of patients experience progression to kidney failure within 3-7 years.
- FSGS may recur a few hours to 2 years after transplant.
- Proteinuria is the only marker that is used to assess the effect from the treatment.

The current Treatment of post transplant recurrent FSGS based on the ASFA guideline

- Management: Steroids, rituximab, and TPE and/or IVIG

- TPE prescription: TPE, lipoprotein apheresis, or IA with regenerative adsorbers can be used; for TPE, plasma volume of 1-1.5 EPV

❖○ Frequency: Daily or every other day

❖○ Replacement fluid: Albumin

❖○ Duration: Three daily TPEs followed by 6 more sessions in the following 2 weeks; for lipoprotein apheresis, 2 sessions per week for 3 weeks followed by 6 weekly treatments

Kashgary et al. BMC Nephrology (2016) 17:104
DOI 10.1186/s12882-016-0322-7

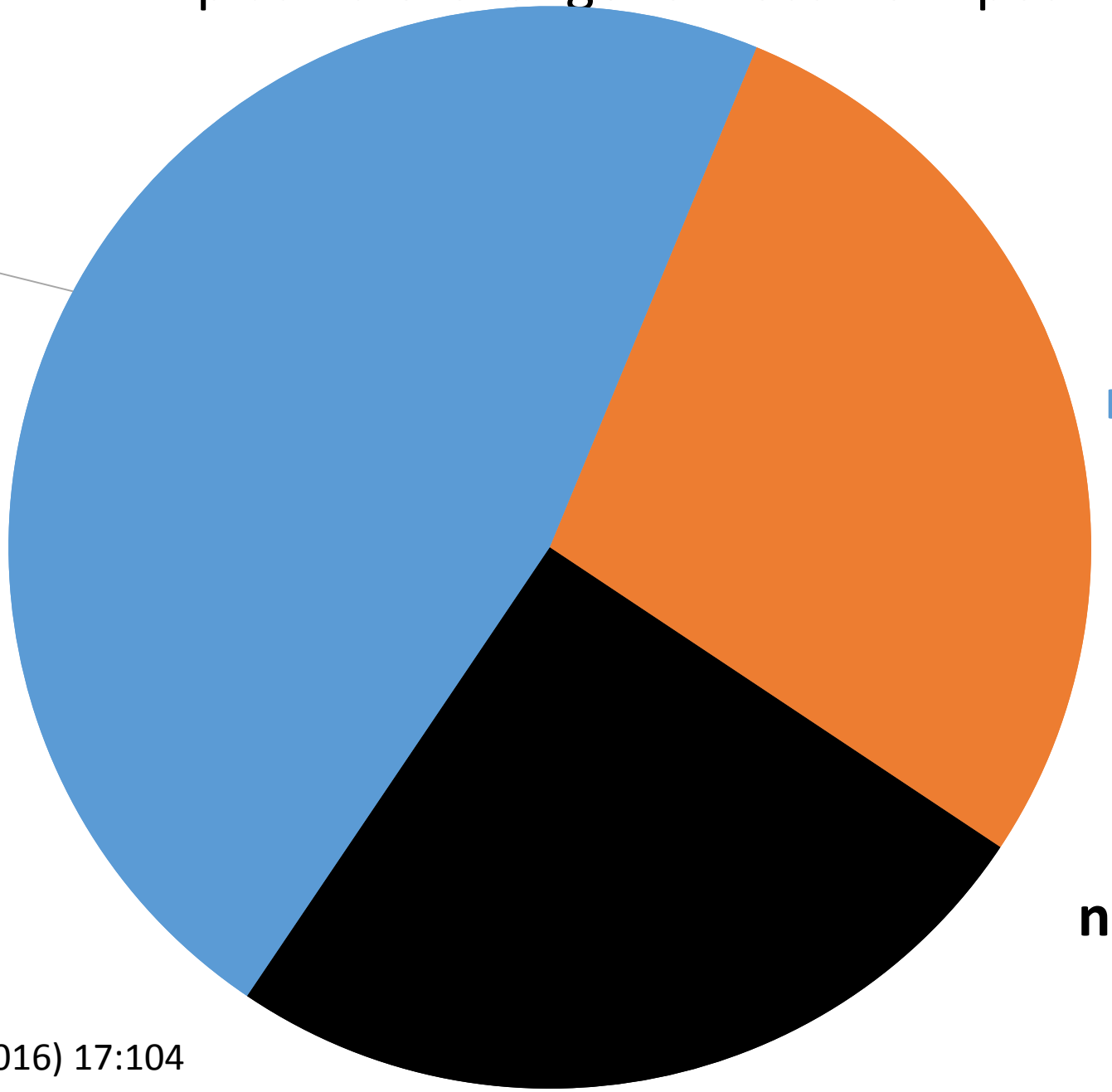
BMC Nephrology

RESEARCH ARTICLE Open Access

The role of plasma exchange in treating post-transplant focal segmental glomerulosclerosis: A systematic review and meta-analysis of 77 case-reports and case-series

Abdullah Kashgary[1,2,5], Jessica M. Sontrop[3,4,5], Lihua Li[4,5], Ahmed A. Al-Jaishi[4,5], Zainab N. Habibullah[1,5], Roaa Alsolaimani[1,2] and William F. Clark[1,4,5*]

Remission after treatment with plasma exchange for recurrent post-transplant FSGS



Kashgary et al. BMC Nephrology (2016) 17:104

Conclusion

- About 75 % of patients achieved full or partial remission from proteinuria after treatment with plasma exchange
- Patients treated within two weeks of recurrence appeared to have a higher likelihood of remission from proteinuria.
- in some cases intensive plasmapheresis for up to several months has been reported

Kashgary et al. BMC Nephrology (2016) 17:104

Desensitization protocols by Therapeutic apheresis

- Desensitization in *ABO-i* kidney transplantation
- Desensitization in patients with preformed *HLA-antibodies*
- Desensitization of *deceased donor* kidney transplant recipients
- Desensitization of *living donor* kidney transplant recipients

Apheresis Tools Available to Desensitize HLA-Incompatible Kidney Transplant Candidates

When the MFI of the DSA is < 3000 before transplant, apheresis is not necessary

Plasmapheresis

- Inexpensive
- Efficient if DSA MFI < 9000
- Many repeated sessions
- Depletion of Ig/clotting factors

Double-filtration plasmapheresis

- Inexpensive
- Efficient if DSA MFI < 12 000
- Many repeated sessions
- Depletion of Ig/clotting factors

Semi-specific immunoadsorption

- Expensive
- Columns adsorbing only Ig
- Many repeated sessions
- Reusable columns
- Efficient if DSA MFI <15,000
- Depletion only of Ig

Experimental and Clinical Transplantation (2018) 4: 367-37

Desensitization in the Setting of HLA-Incompatible Kidney Transplant

Paolo Malvezzi,[1,] Thomas Jouve,[1,2,*] Johan Noble,[1,2] Lionel Rostaing[1-3]*

The target for desensitizing by T.A.

Experimental and Clinical Transplantation (2018) 4: 367-37

Decision making for TPE based on the level of DSA

MFI < 3000 before transplant

Apheresis is not necessary. Prevention of DSA rebound post-transplant is crucial.

MFI ≥ 3000 before transplant

Apheresis should be attempted. Prozone effect elimination is necessary before desensitization. Apheresis should be implemented while the patient is already receiving immunosuppressive drugs.

Experimental and Clinical Transplantation (2018) 4: 367-37

MFI ≥ 3000 before transplant

MFI >3000,≤ 9000

Conventional PP is used.
PP sessions should be performed daily.
Evaluate efficacy after every 5 of PP sessions.
If the DSA MFI does not reduce to < 3000, consider other apheresis techniques

MFI > 9000 and < 13,000:

DFPP can be implemented.
Larger volumes of plasma can be treated compared to PP
DFPP can be used as a starter therapy and converted to PP when the target MFI reaches

MFI > 12,000

Semi-specific Immunoadsorption must be used.
Columns can be reused multiple times.

Experimental and Clinical Transplantation (2018) 4: 367-37

Desensitization in patients with preformed HLA-antibodies

1-Desensitization of deceased donor kidney transplant recipients
2-Desensitization of living-donor kidney transplant recipients

Desensitization of deceased donor kidney transplant recipients

Nephrol Dial Transplant (2002) 17: 1503–1508

Nephrology Dialysis Transplantation

Original Article

Peri-operative immunoadsorption in sensitized renal transplant recipients

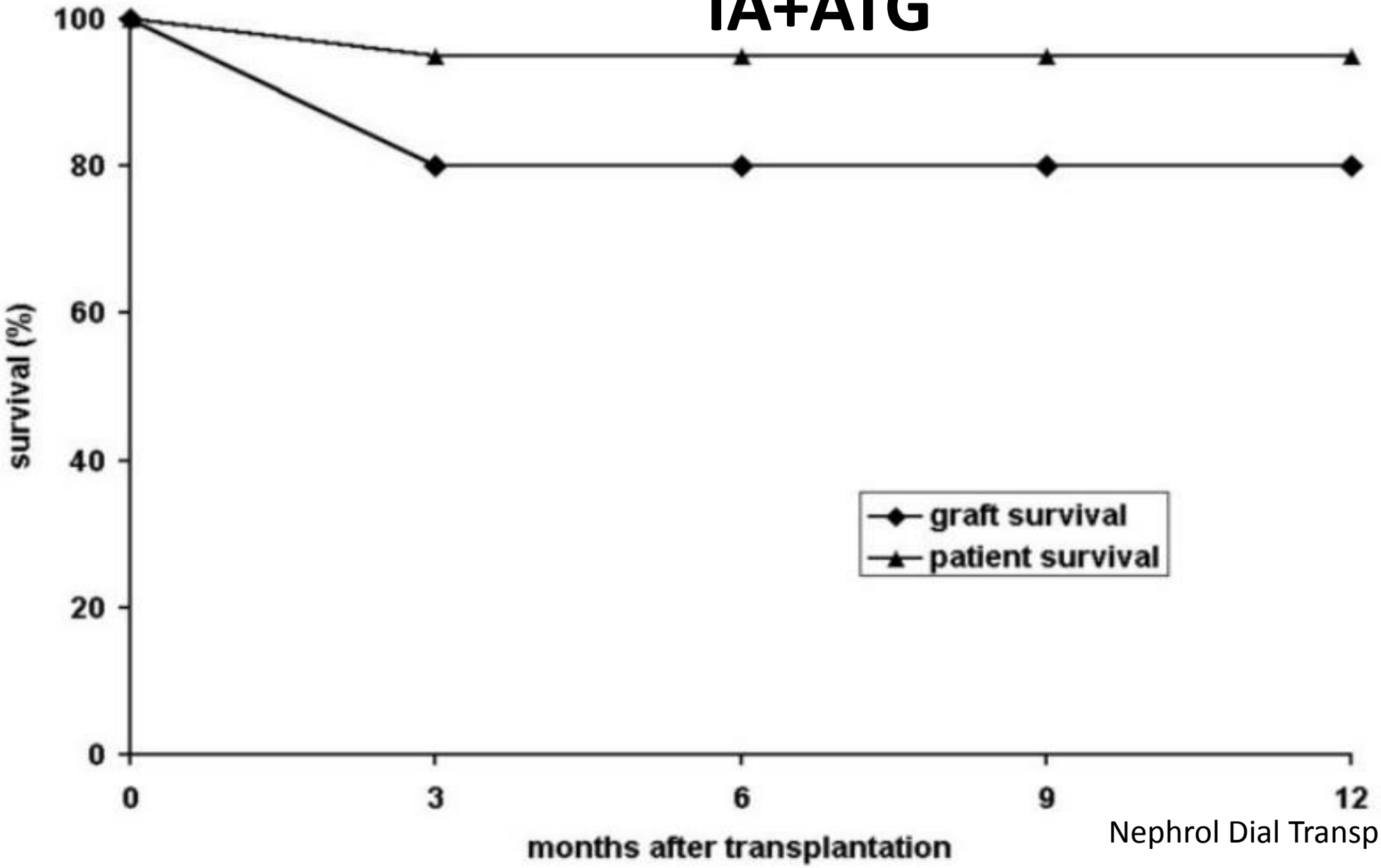
Martin Haas[1], Georg A. Böhmig[1], Zdenka Leko-Mohr[1], Markus Exner[2], Heinz Regele[3], Kurt Derfler[1], Walter H. Hörl[1] and Wilfred Druml[1]

[1]Division of Nephrology and Dialysis, Department of Internal Medicine III, University of Vienna, Austria, [2]Department of Laboratory Medicine, University of Vienna, Austria and [3]Division of Ultrastructural Pathology and Cell Biology, Department of Pathology, University of Vienna, Austria

Nephrol Dial Transplant (2002) 17:1501-1508

Desensitization of deceased donor kidney transplant recipients

IA+ATG



Nephrol Dial Transplant (2002) 17:1501-1508

Conclusion

- The data suggest a beneficial effect of prophylactic peri-operative IA and anti-lymphocyte Ab therapy on graft survival in broadly sensitized renal re-transplant recipients

Nephrol Dial Transplant (2002) 17:1501-1508

Desensitization of Living donor kidney transplant recipients

- The most commonly used protocol is a combination of alternate-day TPE followed by low-dose IVIg (100-150mg/kg) prior to transplantation➔ Initiate Tacrolimus, and MMF up to 2 wk prior to surgery.

Journal of
Clinical Medicine

MDPI

Article

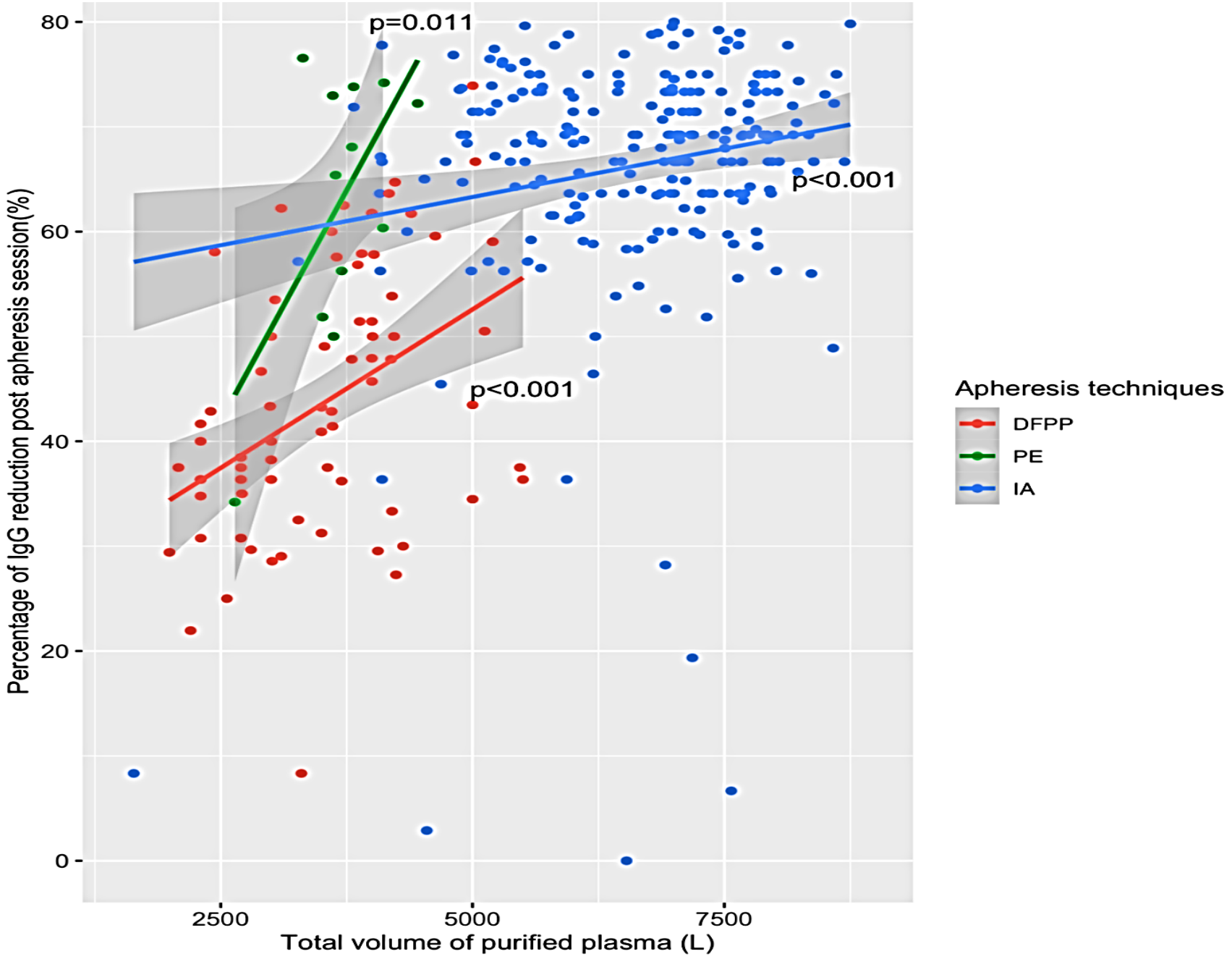
Apheresis Efficacy and Tolerance in the Setting of HLA-Incompatible Kidney Transplantation

Johan Noble [1,2,†], Antoine Metzger [1,†], Hamza Naciri Bennani [1], Melanie Daligault [1], Dominique Masson [3], Florian Terrec [1], Farida Imerzoukene [1], Beatrice Bardy [3], Gaelle Fiard [4,5], Raphael Marlu [6], Eloi Chevallier [1], Benedicte Janbon [1], Paolo Malvezzi [1], Lionel Rostaing [1,2,*] and Thomas Jouve [1,2]

The aim of this study: To assess the efficacy, safety and tolerance of each apheresis technique in the setting of desensitization

J. Clin. Med. 2021, 10, 1316; 1-11

Post session reduction of immunoglobulin-G according to the apheresis technique



J. Clin. Med. 2021, 10, 1316; 1-11

Conclusion

Desensitization with apheresis was effective at removing HLA antibodies and allowed access to HLAi KT for sensitized patients.
IA and PE were more effective to remove IgG and antiHLA antibodies, especially for class II DSAs, and were better tolerated than DFPP.

J. Clin. Med. 2021, 10, 1316; 1-11

TRANSPLANT
INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

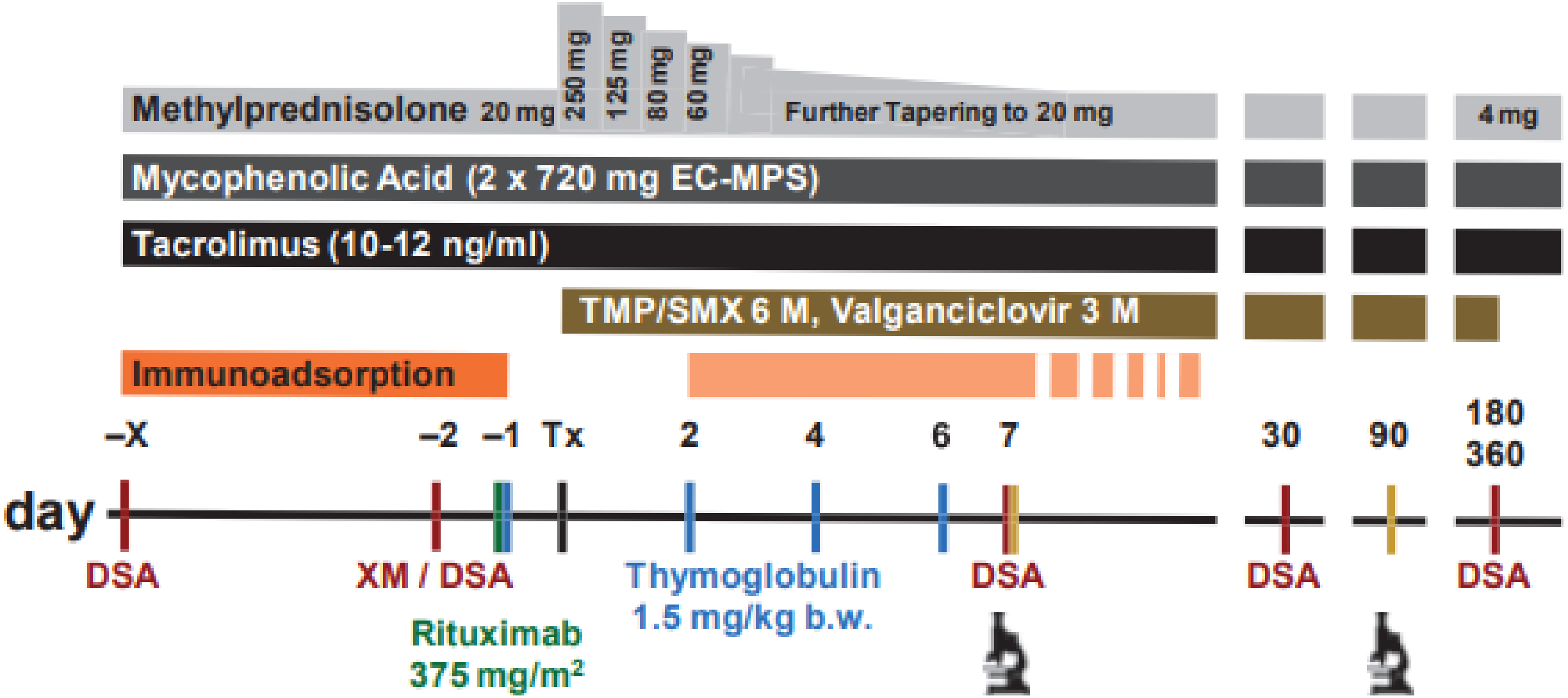
Living donor kidney transplantation in crossmatch-positive patients enabled by peritransplant immunoadsorption and anti-CD20 therapy

Christian Morath,[1] Jörg Beimler,[1] Gerhard Opelz,[2] Sabine Scherer,[2] Jan Schmidt,[3] Stephan Macher-Goeppinger,[4] Katrin Klein,[1] Claudia Sommerer,[1] Vedat Schwenger,[1] Martin Zeier[1] and Caner Süsal[2]

1 Department of Nephrology, University of Heidelberg, Heidelberg, Germany
2 Transplantation Immunology, University of Heidelberg, Heidelberg, Germany
3 Transplantation Surgery, University of Heidelberg, Heidelberg, Germany
4 Department of Pathology, University of Heidelberg, Heidelberg, Germany

Data on a cohort of 10 desensitized living donor kidney recipients with a median of 19 months of follow-up

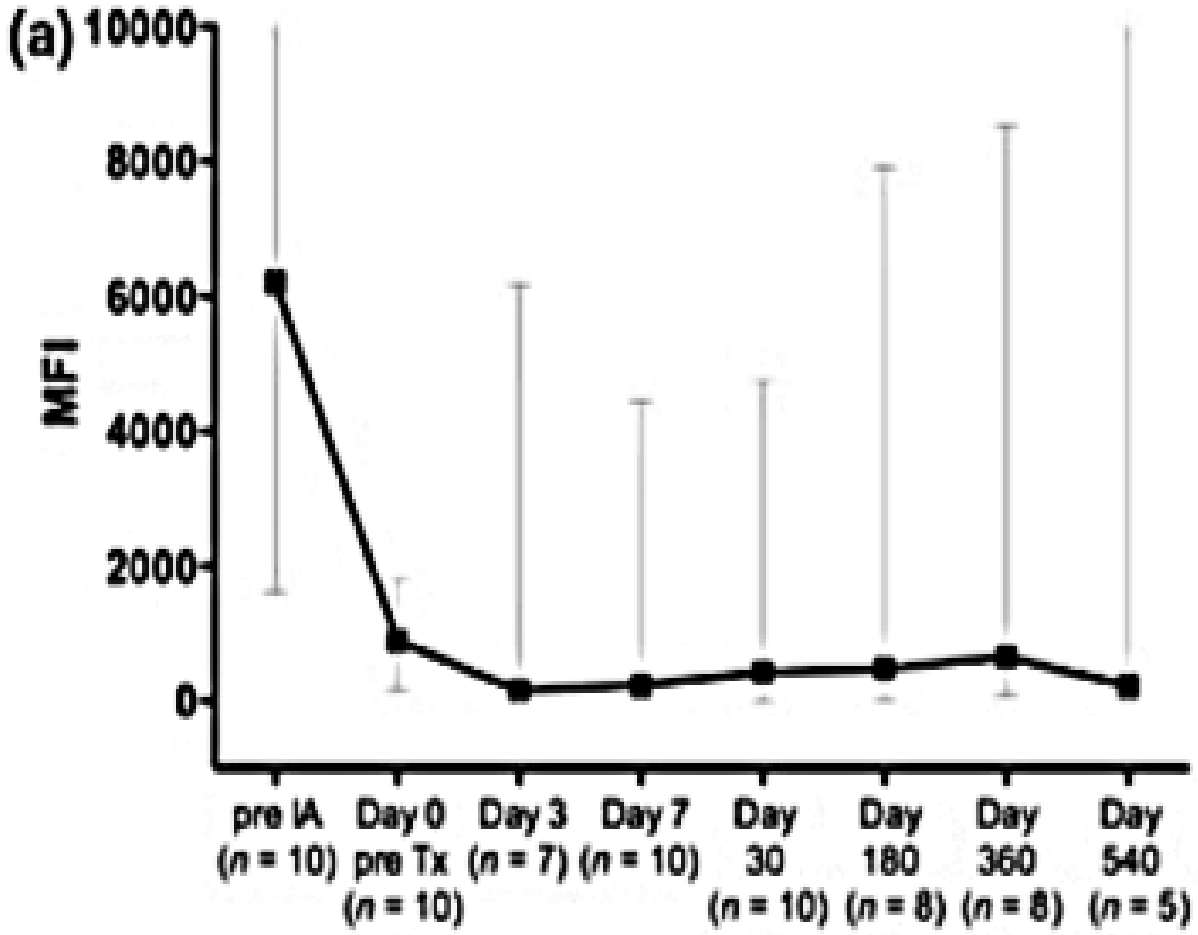
European Society for Organ Transplantation 25 (2012) 506–517

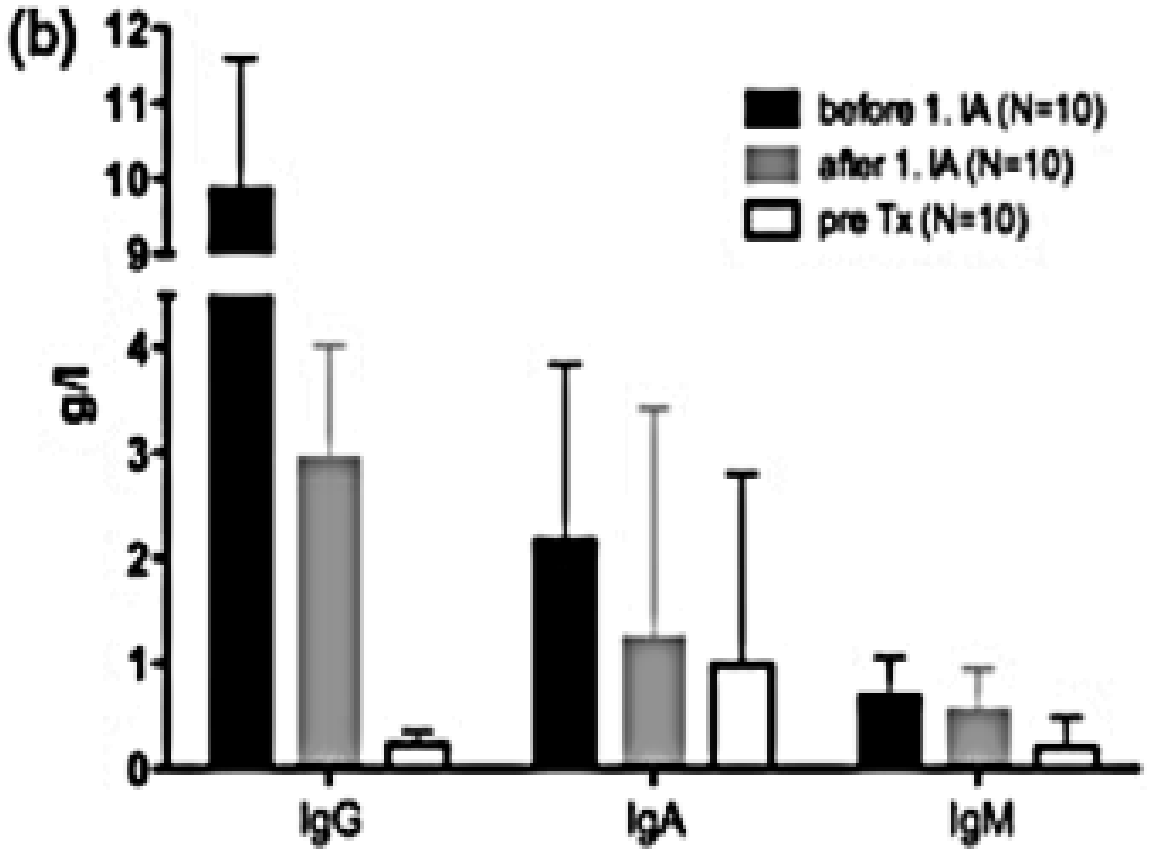


European Society for Organ Transplantation 25 (2012) 506–517

Luminex-detected DSA before transplant IA

Decrease of immunoglobulins during the first and subsequent IA treatments





European Society for Organ Transplantation 25 (2012) 506–517

Desensitization in ABO-incompatible KT

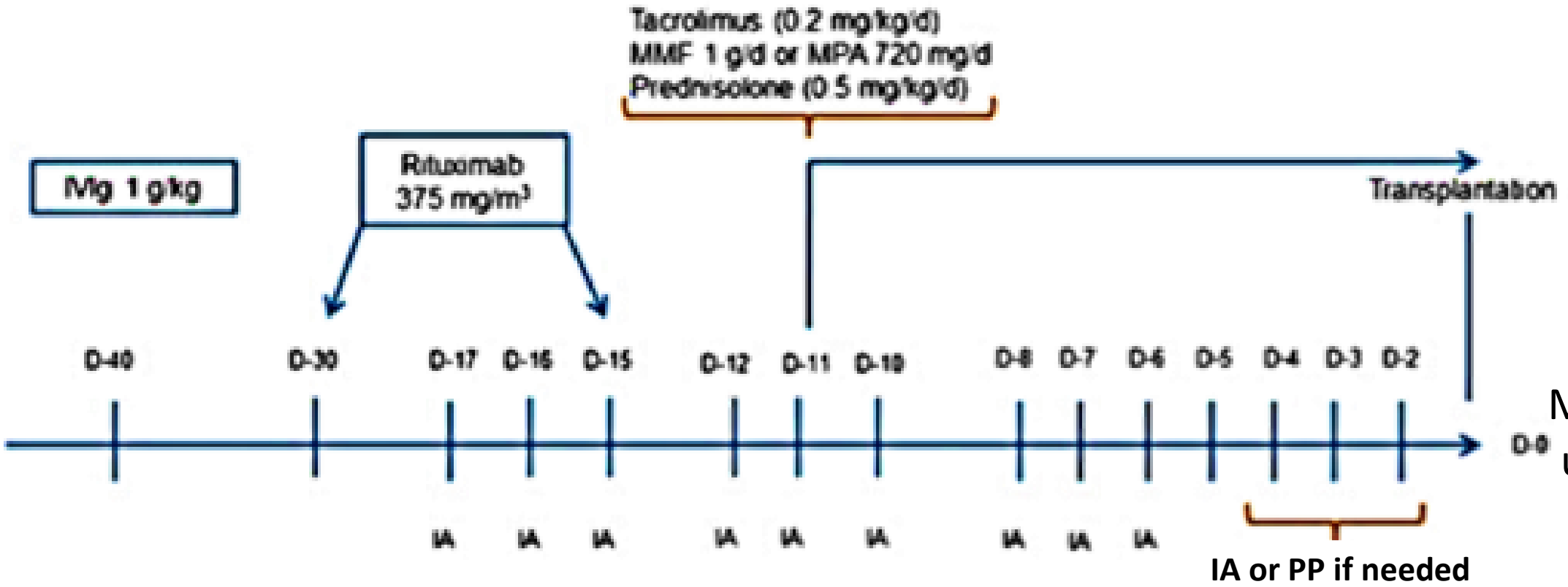
- In patients with baseline titers of ≤ 1:8, apheresis treatment was omitted.
- DFPP was used in those with titers between 1:16 and 1:64
- Antigen-specific IA (glycosorb-ABO IA columns) was used in those with titers above 1:64.

Therapeutic Apheresis and Dialysis

Therapeutic Apheresis and Dialysis 2016; **(**):**–**
doi: 10.1111/1744-9987.12408

Successful Transplantation in ABO- and HLA-Incompatible Living Kidney Transplant Patients: A Report on 12 Cases

Lionel Rostaing,[1,2,3] Béatrice Karam,[4] Nicolas Congy-Jolivet,[3,5] Valérie Hage,[1] Federico Sallusto,[6] Laure Esposito,[1] Nicolas Doumerc,[6] Bénédicte Debiol,[7] Céline Guilbeau-Frugier,[8] Xavier Game,[3,6] Asma Allal,[1] and Nassim Kamar[1,3,9]



Median follow-up 19 months

Patient survival: 100%

→ Graft-survival rates: 91.6%

De novo thrombotic microangiopathy:

1) Drug-induced TMA due to CNI and mTORi➔Alternative IS drugs + PP
2) Ischemia reperfusion injury➔ Conservative treatment+ PP
3) ABMR➔ IVIG+PP➔ Eculizumab
4) Viral infection➔ Antiviral drugs + PP

The current Treatment of post transplant Thrombotic Microangiopathy based on the ASFA guideline

- Management: TPE and/or Eculizumab with immunosuppression
- TA prescription:
  - Plasma volume: 1-1.5 EPV
  - Frequency: Daily
  - Replacement fluid: Frozen plasma or frozen plasma/albumin
  - Duration: Until adequate clinical response or antibody titer reduced to less than clinical threshold (similar to immune TTP)

Post transplantation TTP

- Deficiency of plasma ADAMTS13 activity (<10%) or IgG autoantibodies against ADAMTS13.
- TA aims to remove anti-ADAMTS13 antibodies while replacing ADAMTS13 activity through frozen plasma.

The current Treatment of post transplant TTP based on the ASFA guideline

- ❑ Steroids + TA; adjunct therapies can be used in refractory cases; if rituximab is used, a 24-hour interval should be allowed between infusion and TPE
- ❑ Caplacizumab (a monoclonal antibody against von Willebrand factor) is also available
- ❑ TPE prescription:
  - ❖ ○ Plasma volume: 1-1.5 EPV
  - ❖ ○ Frequency: Daily
  - ❖ ○ Replacement fluid: Frozen plasma
  - ❖ ○ Duration: Daily until platelet count is >150 × 103 /µL and LDH level is near normal for 2-3 consecutive days

Antiphospholipid syndrome and systemic lupus erythematosus

- graft thrombosis takes place in 40% of the APS population despite anticoagulant therapy.
- Catastrophic APS (CAPS), which is characterized by diffuse TMA (vascular occlusions involving three or more organ systems)➔ prophylactic administration of eculizumab to prevent recurrence of CAPS after KT should be considered the preferred therapeutic option.
- PP can be used as prophylaxis when eculizumab is not available.
- The procedure should be performed in combination with steroids ± IVIG and anticoagulants

Recurrent and de novo anti-glomerular basement membrane Dis.

- The histological recurrence of Anti-GBM may be as high as 50% in patients who receive a transplant while circulating anti-GBM antibodies persist.
- TA should be used promptly to remove the causative antibody plus glucocorticoids and cyclophosphamide to inhibit further autoantibody production.
- PEX is performed daily or every other day, anti-GBM antibody titers should be monitored and the procedure should be performed until the autoantibodies are undetectable (approx. 10–14 sessions)

Recurrence of ANCA-associated vasculitis

- It is a rare event after transplantation, because transplantation should be delayed until a complete extra-renal remission for at least 12 months is achieved.
- TPE is recommended, in conjunction with glucocorticoids and either cyclophosphamide or RTX in the setting of alveolar hemorrhage, severe segmental necrotizing glomerulonephritis with cr>4.0 mg/dL, and concurrent anti-GBM disease.

Conclusion

- Multiple types of TA are used in the renal transplantation, based on the diseases type and facilities in each center.
- The common indications for plasmapheresis in renal transplantation are the management of ABMR, FSGS, TMA, and desensitization protocol.
- TA is typically used with accompanied of the other immunosuppressive drugs, such as corticosteroids, intravenous immunoglobulins, and anti-rejection medications.
- Potential complications include fluid and electrolyte imbalances, infection, bleeding, and reactions to the replacement fluids.
- The COST/BENEFIT ratio should be considered in the any case.

Thank you for your attention