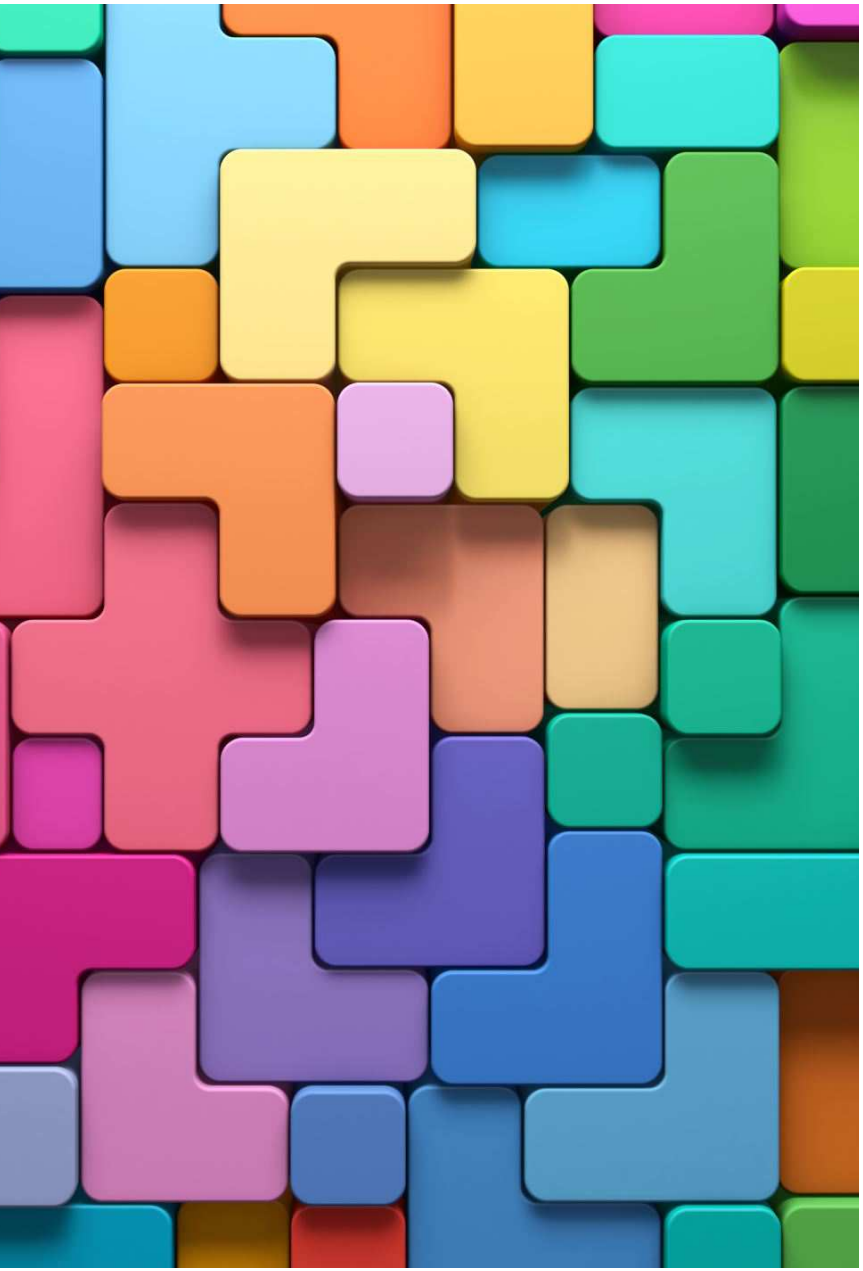


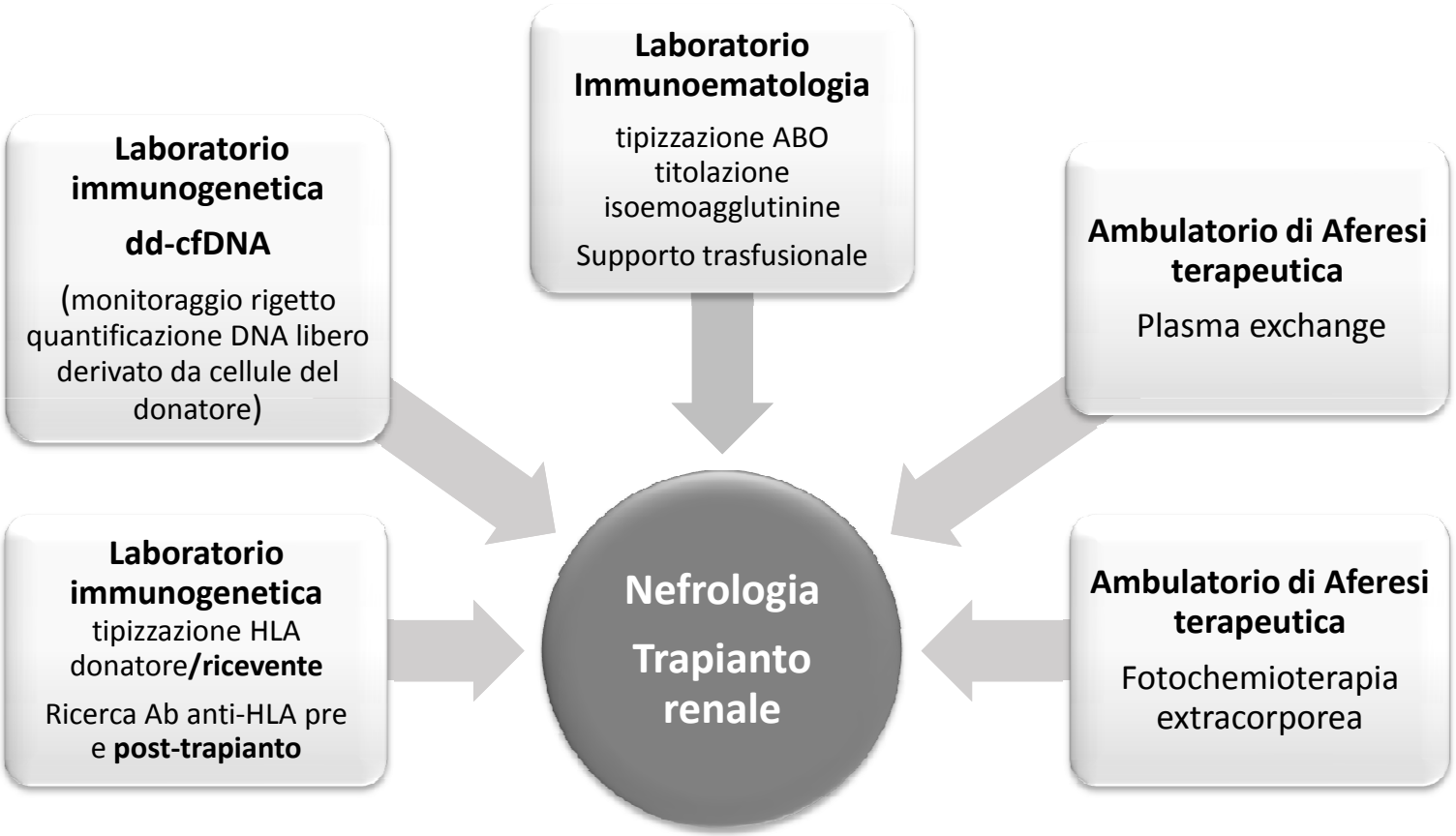
TRENT'ANNI DI TRAPIANTO RENALE
A UDINE E IN FRIULI VENEZIA GIULIA

Udine, 30 giugno 2023

Laboratorio Immunotrasfusionale
al servizio del trapianto
e
metodiche aferetiche nella sua gestione

Dott.ssa Chiara Savignano
SOC Medicina Trasfusionale
ASUFC Udine

Il ruolo della Medicina Trasfusionale nella gestione del trapianto renale



Il laboratorio di Immunoematologia nel trapianto di Rene

Il Laboratorio di Immunoematologia esegue:

- tipizzazione ABO del ricevente (e del donatore)
- ricerca delle isoemagglutinine (anti-A, Anti-B).

Trapianto rene ABOi

Gli antigeni A e B sono fortemente espressi sia a livello endoteliale che tissutale nel rene trapiantato e la presenza dei corrispettivi anticorpi anti-A/anti-B nel plasma del ricevente può scatenare quadri di rigetto iperacuto .

il **superamento della Barriera ABO** richiede la rimozione delle isoemoagglutinine.

Titolazione Ab anti-A/anti-B:

- titolazione prima del trapianto
- verifica raggiungimento titolo soglia il giorno del trapianto
- monitoraggio titolo post-trapianto

Valore soglia pre trapianto: anti-A/B IgM < 1:8; anti-A/B IgG <1:8

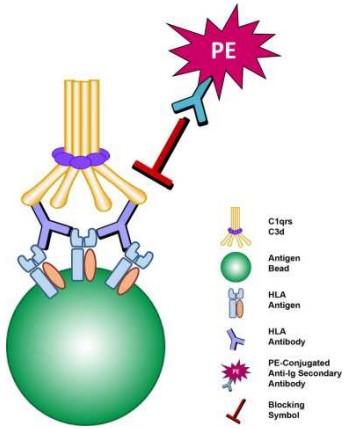
D. Londero

Il laboratorio HLA nel trapianto di Rene

Il Laboratorio di Immunogenetica (HLA) è coinvolto in tre fasi:

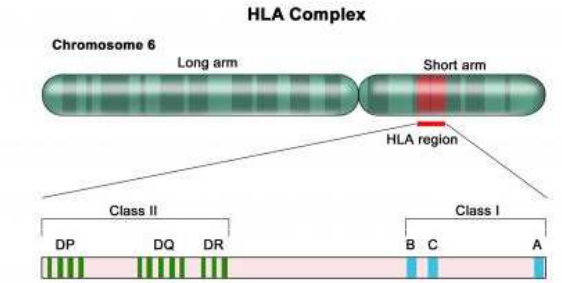
Pre-Trapianto

-Tipizzazione HLA Donatore/Ricevente
-Studio anticorpale anti-HLA del ricevente



Trapianto

-Crossmatch
(siero Ricevente/linfociti B,T Donatore)



Post-Trapianto

-Monitoraggio DSA
-dd-cfDNA

D. Londero

ASU FC
Azienda sanitaria universitaria Friuli Centrale

REGIONE AUTONOMA FRIULI VENEZIA GIULIA

Il laboratorio HLA nel trapianto di Rene

- **Tipizzazione HLA del ricevente/donatore ai fini della valutazione della compatibilità:** i dati di letteratura dimostrano la chiara correlazione tra grado di compatibilità e sopravvivenza d'organo.
- La tipizzazione HLA del ricevente riguarda i loci **HLA-A, -B, -C, -DRB1, -DQB1** (nei riceventi sensibilizzati estensibile a **loci** DQA, DPA, DPB) e si effettua con tecniche genomiche a bassa risoluzione
- **Studio dello stato di pre-sensibilizzazione HLA:** la presenza di anticorpi anti-HLA donatori-specifici (DSA) «citotossici», cioè fissanti il complemento è associato a una perdita precoce dell'organo. Nei pazienti candidati al trapianto viene effettuata la ricerca e caratterizzazione degli anticorpi **anti-HLA di classe I e di classe II** in fase solida, permettendo una valutazione semiquantitativa (MFI) dell'anticorpo evidenziato (**Cut-off positività>3000 MFI)**
- Si esegue di norma:
  - al momento dell'iscrizione in lista di attesa,
  - successivamente ogni tre mesi, a 20 giorni/1 mese di distanza da eventi sensibilizzanti
  - nel follow up post trapianto (fenomeni di rebownd / de novo_DSA) .

LINEE GUIDA AIBT per la Valutazione dell'Istocompatibilità nel Trapianto d'Organo (in sinergia con SITO-2016)

D. Londero

ASU FC
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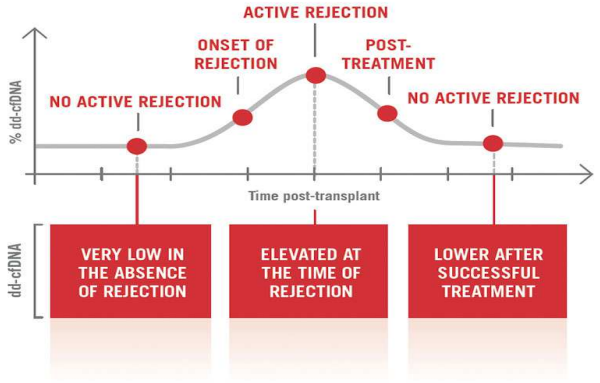
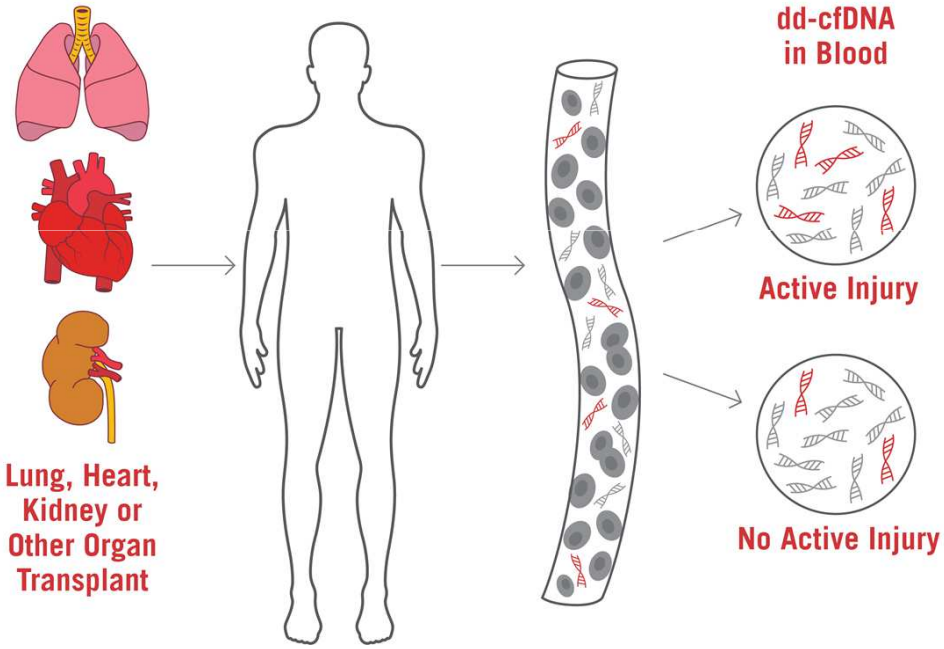
REGIONE AUTONOMA FRIULI VENEZIA GIULIA

Rilevazione del cell-free DNA derivante da donatore

Quantificazione nel plasma del ricevente del DNA libero circolante derivato dal donatore, proveniente da cellule che vanno incontro a danno/morte cellulare. Aumenta in presenza di rigetto d'organo e viene utilizzato:

- **Sorveglianza del rigetto**
- **Follow-up trattamento post-rigetto**





Ruolo delle tecniche aferetiche nel trapianto renale

Therapeutic Apheresis in Transplantation Medicine

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice from the Writing Committee of the American Society for Apheresis: Ninth Issue (2023)

Disease/condition	Indication	Procedure	Category	Grade	Page
Transplantation, heart	Cellular rejection	ECP	II	1B	249
	Recurrent rejection	ECP	II	1B	
	Rejection prophylaxis	ECP	II	2A	
	Desensitization	TPE	II	1C	
	Rejection prophylaxis[a]	TPE	II	1C	
	Antibody mediated rejection	TPE	III	2C	
Transplantation, hemapoietic stem cell, ABO incompatible	Major ABO incompatible, HPC(M)	TPE	II	1B	251
	Major ABO incompatible, HPC(A)	TPE	II	2B	
	Minor ABO incompatible, HPC(A)	RBC exchange	III	2C	
	Pure red cell aplasia	TPE	III	2C	
Transplantation, hematopoietic stem cell, HLA desensitization		TPE	III	2C	253
Transplantation, intestine[a]	Antibody mediated rejection	TPE	III	2C	255
	Desensitization	TPE	III	2C	
Transplantation, kidney, ABO compatible	Antibody-mediated rejection	TPE/IA	I	1B	257
	Desensitization/prophylaxis, living donor	TPE/IA	I	1B	
Transplantation, kidney, ABO incompatible	Desensitization, living donor	TPE/IA	I	1B	259
	Antibody mediated rejection	TPE/IA	II	1B	
Transplantation, liver	Desensitization, ABOi, living donor	TPE	I	1C	261
	Desensitization, ABOi, deceased donor	TPE	III	2C	

Therapeutic Apheresis Tecniques performed in the setting of kidney transplantation

Procedure	Tecniques	Mechanism of action
Therapeutic plasma exchange	Patient plasma is separated from other components of blood, by membrane filtration (mTPE) or centrifugation (cTPE). The plasma is removed with subsequent substitution of a replacement solution. (albumin /FFP)	Removal of high-molecular – mass substances (15.000D) such pathological antibodies, immune complex, paraproteins, cytokines and adhesion molecules Immunomodulathory effect : decline in B and NK cells ; incease in T suppressor cell function
Double filtration plasmapheresis	two-step procedure: Membrane plasma separation is followed by plasma filtration	Removal of targeting portions of plasma components (immunoglobulin) on the basis of molecular weight and three-dimensional structure.
Immunoadsorption	A selective method in which patient plasma, after membrane based or centrifugal separation from blood, is passed through an adsorber column which has a capacity to remove immunoglobulins and immune complexes by binding them to select ligands	Selective binding of circulating molecules: - Anti-IgG antibodies (Thera SorbTM-ig) - staphylococcal Prot A (high avidity for the Fc portion of IgG1, IgG2,IgG 4) - antigen/syntetic epitopes
Extracorporeal Photopheresis	Collection and photo-inactivation of the blood mononuclear cells fraction subsequently reinfused to the patient.	Immunomodulathory (tholerogenic) effect: - suppress the activity of effector T cells - induce the production of regulatory T cells (Tregs) - Increase anti inflammatory cytokine release (IL10, TGF-beta - Decrease in pro inflammatory cytokine realease (IL 1alfa, Il 6)

Indication for TA in Kidney transplantation

Clinical indications	Procedure
Desensitization in ABO-i Kidney transplantation	IA/TPE
Desensitization in patients with preformed HLA antibodies	TPE/IA
Desensitization of deceased donor kidney transplant recipients	TPE/IA
Desensitization of living donor kidney transplant recipients	TPE/IA
Antibody mediated rejection (AMR)	TPE
Recurrence of primary FSGS	TPE
Recurrence of complement mediated aHUS	TPE
De novo TMA	TPE
Cronic active AMR , cellular rejection	ECP

Salvadori M *et al. World J Transplant* 2019 October 28; 9(6): 103-122

Desensitization in ABO-i Kidney transplantation

	ISS	TA tecnique	Initial Titers	Schedule
Tyden et al Transplantation 2003	Rituximab	Immunoadsorbtion (Glycosorb ABO column)	> 1:8	Pre Tx: -6,-5,-4,-1 Post Tx: +3,+ 6,+9
Barnet et al Transplantation Int 2014	Rituximab (only for isoemaglutinines titers >16)	- Double Filtration PE Immunoadsorbtion	< 1:8 1:8- 1:64 > 1:64	No treatment Pre-Tx: 2-3 proc. Pre-TX: 2-3 proc Post Tx: on demand

Tailoring the intensity according to individual immunological risck shoul be the recommended strategy

Salvadori M *et al. World J Transplant* 2019 October 28; 9(6): 103-122

Desensitization in patients with preformed HLA antibodies

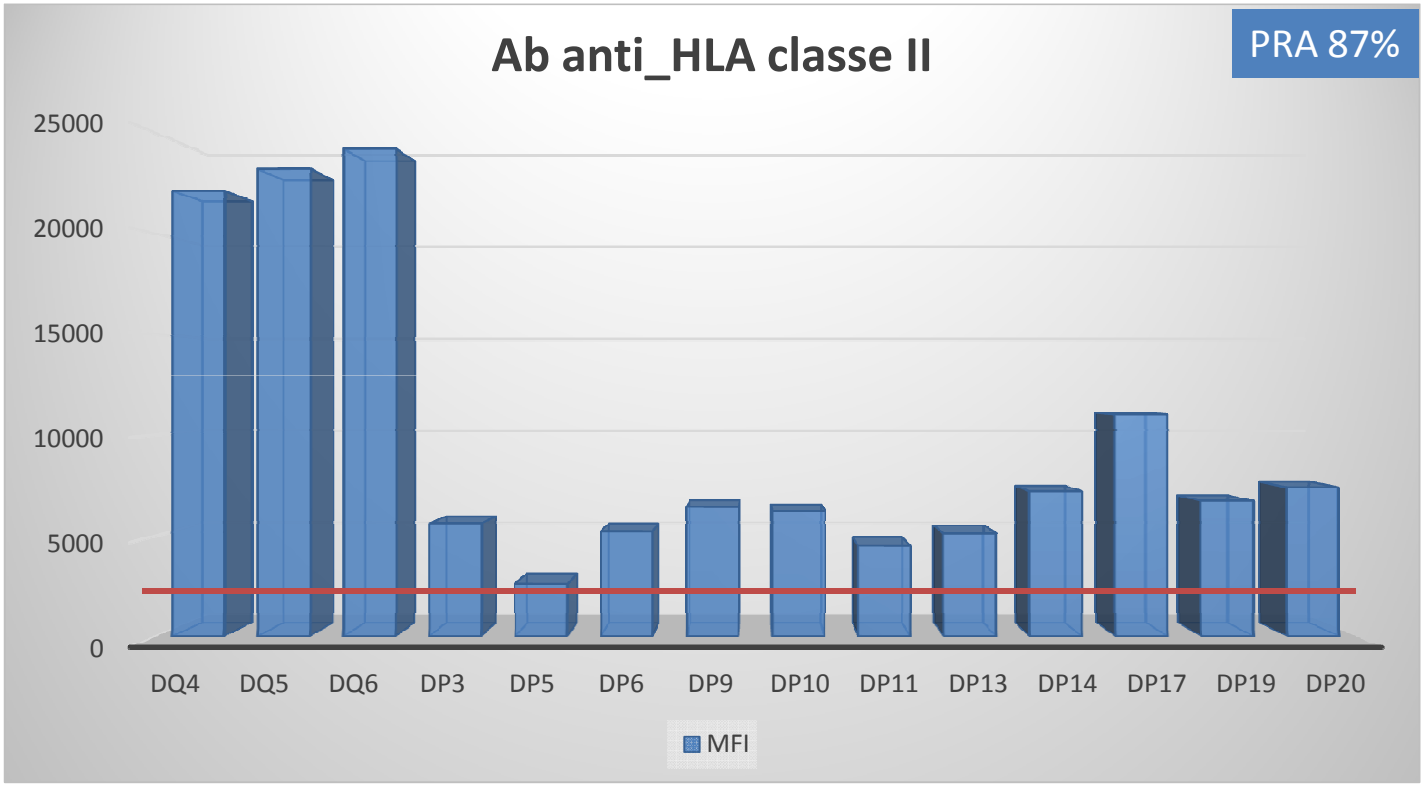
- Preformed anti-HLA antibody represent a major immunological barrier to successful KT
- transplanting a kidney into a recipient with strong pre-existing donor specific antibodies (DSA) is associated with acute antibody mediated rejection , chronic humoral rejection and poor allograft outcomes
- Approximately 30% of the KT candidates have detectable anti-HLA antibodies and approximately half of them are “highly”sensitized with HLA antibody reactivity panel to over 80% of potential donors
- Patients with high calculated panel reactive antibody (cPRA) score (>80%) have difficulty finding HLA compatible donors and remain on the transplantation list significantly longer than unsensitized patients

Desensitization in patients with preformed HLA antibodies

- Desensitization regimens typically include TPE/ IA , IVIG, rituximab, ± additional ISS induction therapy
- Target: reducing antibody levels to a predetermined MFI cut-off or converting a positive flow crossmatch result to negative prior to transplant
- **Desensitization of deceased donor KT recipients**
  - **Pre-transplant**: in candidates on the waiting list to increase the chances of finding an acceptable donor (strategies not always effective)
  - **Peri-transplant**: in patients with negative or positive cross match and elevated DSA titers (1 to 9 PEX procedures + IVG/RTX or ATG)

- **Desensitization of living donor KT recipients**
  - alternate day PEX followed by low dose IVIg (100-550 mg/kg) +/- rituximab prior to transplantation (4-5 proc).
  - ISS therapy (Tac, MMF) start : 2 wk prior surgery
  - Alternate day PEX post transplant (5-9 proc)
  - Induction therapy : ATG or basiliximab

Caso Clinico



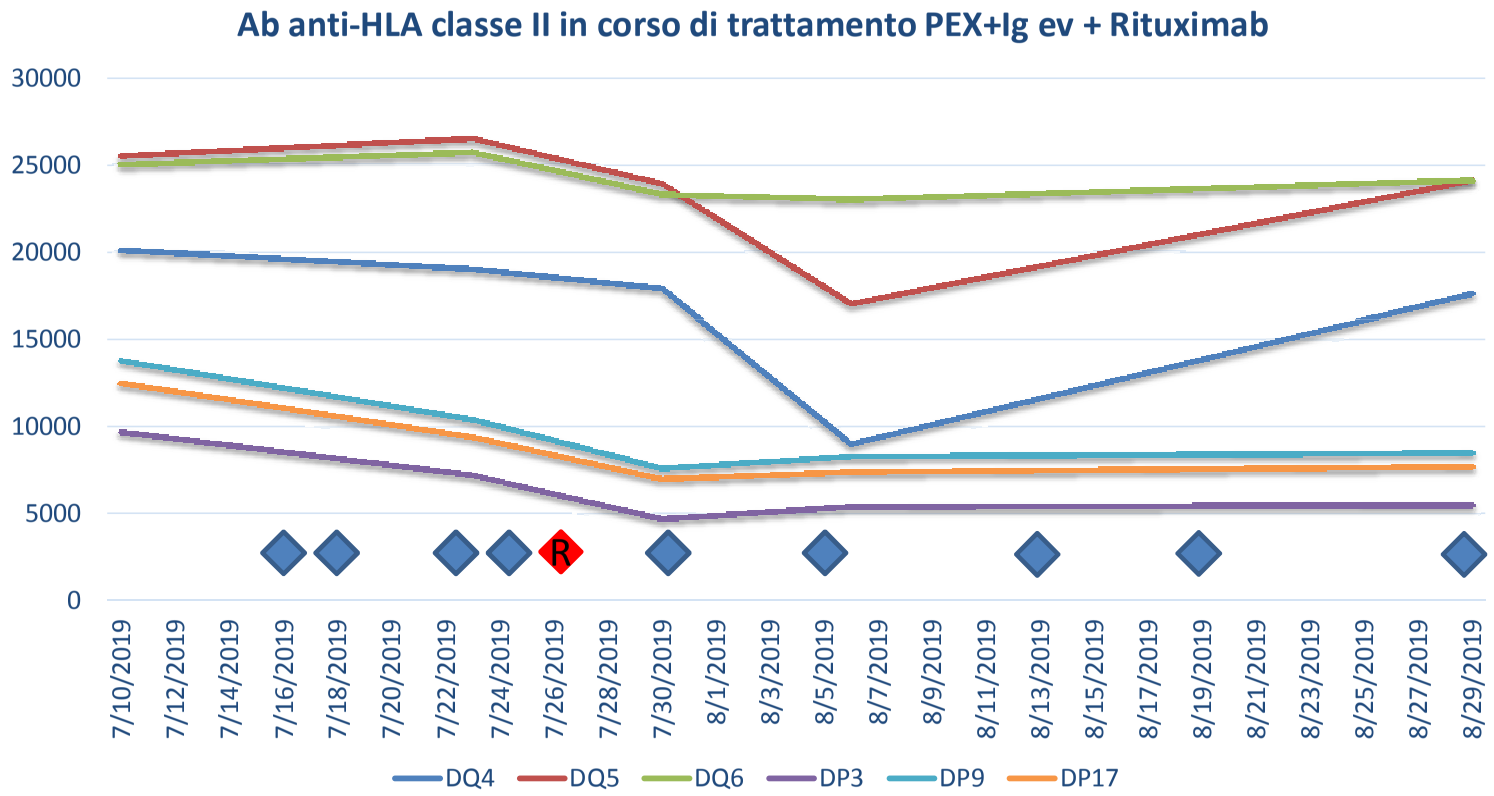
Pz F, aa 38

Diagnosi : candidata a retrapianto cuore rene (scompenso cardiaco dx e IRC dialisi dip).

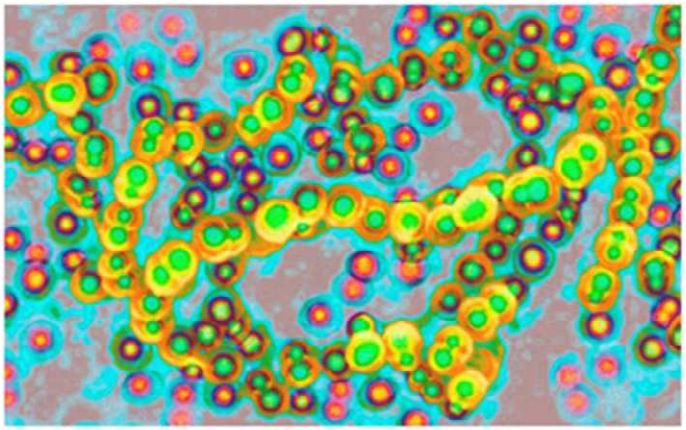
In anamnesi:
I trapianto cuore-rene 1997
II trapianto rene 2012

In lista trapianto da 24 mesi

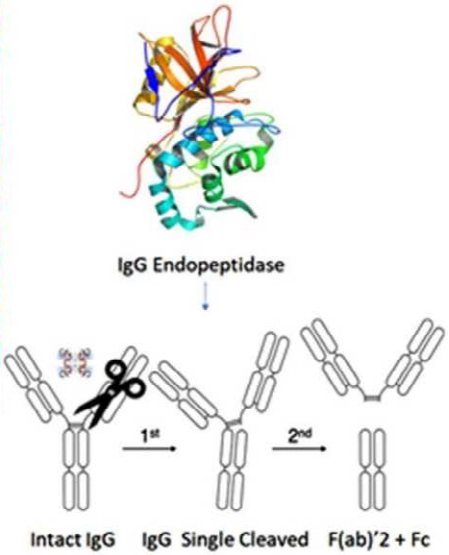
Caso Clinico



IMFLIMIDASE



Streptococcus Pyogenes



- Recombinant cysteine protease derived from *S. pyogenes*
- has the capacity to cleave all four human subclasses of IgG with precise specificity
- The removal of Fc fragments completely inhibits IgG-mediated complement-dependent cytotoxicity (CDC) and antibody-mediated cellular cytotoxicity (ADCC)

AIFA approved, G U n.286 7-12-2022

Patients selection criteria:

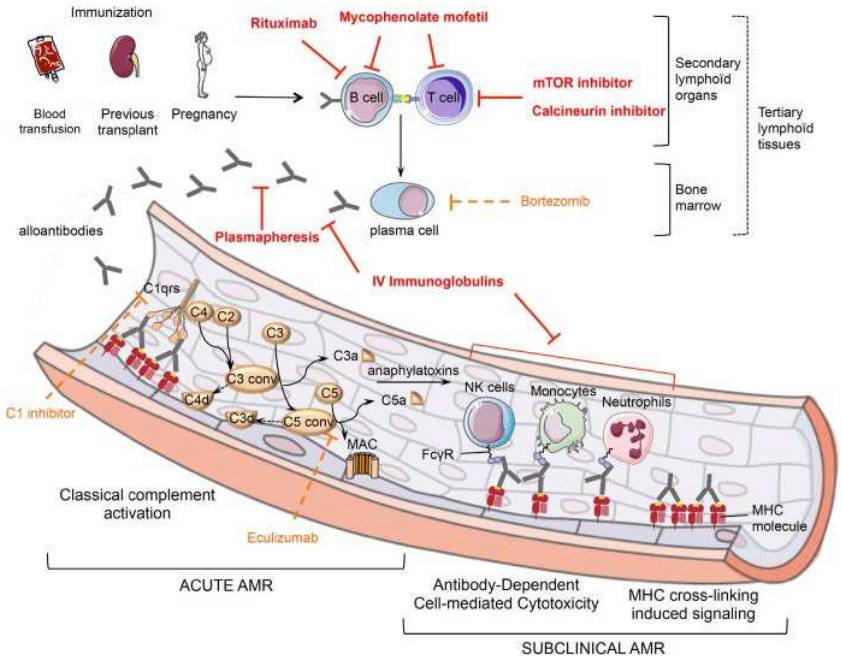
- Dialisis > 4 years
- PRA/cPRA > al 90%
- positive cross match,

Dose 0.25 mg/kg before transplant

Effect: Within six hours of treatment, there was near-complete elimination of DSA in all patients

Concern: DSA rebound (day +3 -+6)
infections

Antibodies mediated rejection



Antibody-mediated rejection (AMR) is the most common cause of graft loss after kidney transplantation

On the basis of Banff 2019 classification, 3 diagnostic AMR categories are recognized:

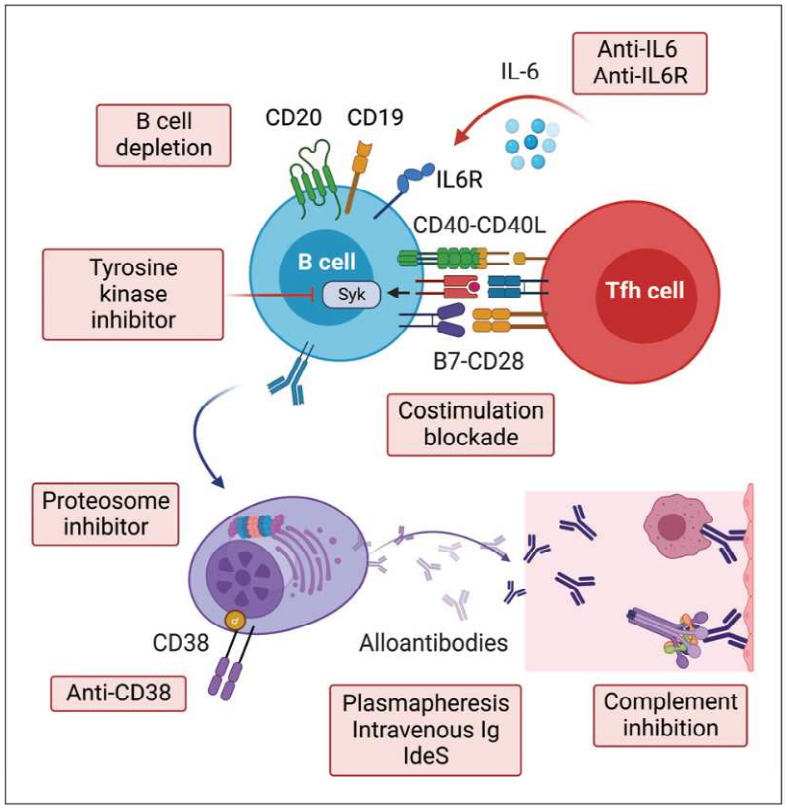
- Active AMR (early and late),
- Chronic active AMR
- Chronic AMR

Donor-specific antibody (DSA) is an independent risk factor for active AMR:

- Preformed DSA
- De novo DSA: in 15–25% of KT recipients within the first 5 years

There are several published randomized clinical trials evaluating treatment regimens in AMR in kidney transplant recipients . However, most had small sample sizes and were underpowered to find differences between treatment regimens

Currently used and investigational drugs for kidney transplant recipients with antibody-mediated rejection.



Drug	Drug composition	Target	AMR type
Rituximab	Anti-CD 20	B cells	Active AMR
Eculizumab	Anti-CF C5a	Complement inhibition	Active AMR
Imilfidase	IgG endopeptidase	Antibody cleavage	Active AMR
Bortezomib	proteasome inhibitor	Plasma cells	Chronic Active AMR
Tocilizumab	Ab anti-IL-6 receptor-α	Plasma cells	Chronic Active AMR
Clazakizumab	Ab anti-IL-6	Plasma cells	Chronic Active AMR
Felzartamab	Ab anti-CD38	B cells and plasma cells	Late AMR
Fostamatinib	Tyrosine kinase inhibitor	T and B cells	Chronic Active AMR

Evidence for use of plasma exchange and IGEv as Standard of Care in active AMR

Criterion	Evidence	Reference
Biological rationale	to combine removal of circulating DSA with mmunomodulation of the antigraft immune response and in particular modulation of the B-cell response (Ig Ev have pleiotropic effects including neutralization of antibodies, cytokines, activated components of complement, effects on B cells, T cells, and Fc receptors)	Akiyoshi et al 2012 Gelfand et al 201264
Benefit in clinical (observational) studies	The treatment with PE/IVIG results in improved renal function and better graft survival. Their ability to improve short-term outcomes has been demonstrated by several studies, while their results on long-term effects remain variable	Rocha et al 2003 Lefaucheur et al 2009
International recommendations	**KDIGO 2010**: Recommendation for PE and IVIG in association with corticosteroids **BTS 2015** Guidelines for Antibody Incompatible Transplantation **FDA 2017** Public workshop: Antibody removal therapies, generally in combination with low- or high-dose IVIG (immunomodulation) form the SOC in many institutions. **Transplantation Society Working Group 2020** Recommended Treatment For Antibody-mediated Rejection After Kidney Transplantation **ASFA Guidelines for Therapeutic Apheresis 2023** : TPE (cat I /cat 1B)+ Ig ev	Kasiske et al 2010 Velidedeoglu et al2018 Schinstock 2020 2023
Most used combination in clinical practice	American Society of Transplantation survey: Most centers utilize a combination of IVIG and plasmapheresis for treatment. The treatment of AMR in kidney transplant recipients: a systematic review	Burton et al 2015 Wan et al 2018

Carrie A. Schinstock, MD, *Transplantation* 2020;104: 911–922), modified.

AMR : Consensus treatment recommendations based on available evidence and expert opinion

Timing	DSA	Histology (Banff 2017)	Standard of care[a]	Consider adjunctive therapies
Early[a] Acute (<30 days posttransplant)	Preexisting DSA (or nonimmunologically naive)	Active AMR	Plasmapheresis (daily or alternative day × 6 based on DSA titer) (1C)[b] IVIG 100 mg/kg after each plasmapheresis treatment or IVIG 2 g/kg at end of plasmapheresis treatments (1C) Corticosteroids (EO)	Complement inhibitors (2B) Rituximab 375 mg/m^2 (2B) Splenectomy (3C)
Late (>30 days posttransplant)	Preexisting DSA	Active AMR	Plasmapheresis (daily or alternative day × 4–6 based on DSA titer) (2C)[b] IVIG 100 mg/kg after each plasmapheresis treatment or IVIG 2 g/kg at end of plasmapheresis treatments (2C) Corticosteroids (EO)	Rituximab 375 mg/m^2 (2B)
		Chronic AMR	Optimize baseline immunosuppression (eg, add steroids if on a steroid-free regimen) (1C)	IVIG (3C)
	De novo DSA	Active AMR	Optimize baseline immunosuppression (eg, add steroids if on a steroid-free regimen) (1C) Evaluate and manage nonadherence	Plasmapheresis and IVIG (3C) Rituximab (3C)
		Chronic AMR		IVIG (3C)

[a]For all cases, treatment of concomitant T-cell–mediated rejection (≥borderline) and optimizing immunosuppression is recommended. Optimizing immunosuppression includes the use of tacrolimus with goal trough of >5 and use of maintenance steroid equivalent to prednisone 5 mg daily.
[b]Fresh-frozen plasma to be used for replacement fluid for plasmapheresis if a biopsy was performed within 24–48 h. The codes for grades of evidence have been taken from KDIGO.[54,56]
AMR, antibody-mediated rejection; DSA, donor-specific antibody; EO, expert opinion; IVIG, intravenous immune globulins; KDIGO, Kidney Disease: Improving Global Outcomes.

Schinstock 2020, Transplantation, May 2020: 104 /5

Aferesi Terapeutica
Esperienza della Medicina Trasfusionale di Udine

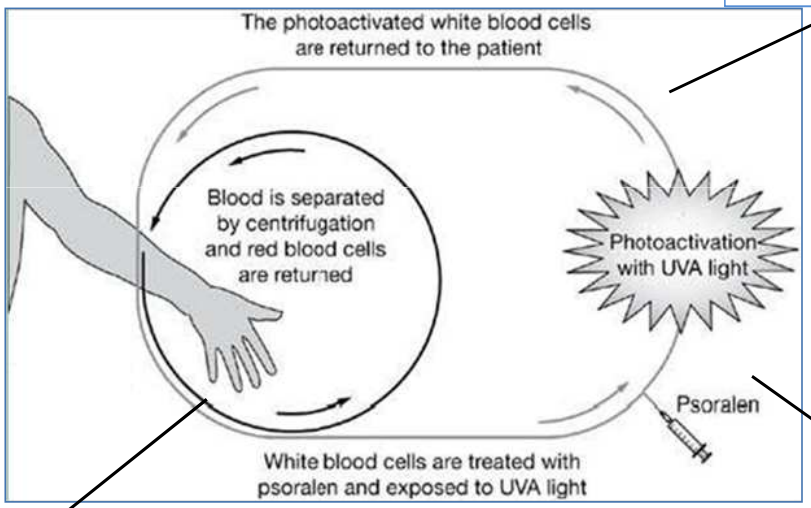
Periodo : 2012-2022
N° pazienti: 41
N° procedure PEX: 286

Parametri	**Rigetto anticorpo mediato (AMR)**		**Desensibilizzazione in presenza DSA**	**Recidiva GSF**	**TMA rene trapiantato**
	acuto	cronico attivo			
N° pz	3	13	19	3	2
Età	60 (59-61)	51 (25-71)	52 (33-71)	57 (40/70)	42-65
M/F	3/1	7 / 6	9/10	2/1	0/2
N° trapianto I° II° III°	3	11 2	5 10 4	2 1 -	2 - -
Mediana proc /pz	5 (4-10)	8 (4-16)	5 (1-16)	5 (5-9)	1-8

ECP - Extracorporeal photopheresis

immunomodulatory cell therapy

3 Re-infusion of treated MNC cells into the patient.



1 Collection of mononuclear cells

2 Photoactivation : 8 MOPP + UVA

ECP- MNC COLLECTION

1. **In-line: integrated systems for cellular collection, photoactivation, and infusion** (THERAKOS® CELLEX® /AMICUS® Blue)
2. **Off-line: ell collection devices** (OPTIA® Terumo BCT) + authomated photoactivation devices

Table 1: Comparison between "In-Line" and "Off-Line" Method of ECP

Parameters	"In-Line" Method		"Off-Line" Method
	UVAR-XTS	CELLEX	
Main Principle	Integrated system on single instrument	Integrated system on single instrument	Separate Instrument for each step
UV-A Dose	1.2 J/cm^2	1.2 J/cm^2	2 J/cm^2
Apheresis Technique	Discontinuous	Discontinuous or Continuous	Continuous
Venous Access	Single	Single or Double	Double
Anticoagulant	Heparin	Heparin	ACD
QC of cells	No	No	Yes
Duration	1.5-2 hours	1.5-2 hours	3-4 hours
Pediatric Use	No	Yes: Weight >40 Kg	Yes

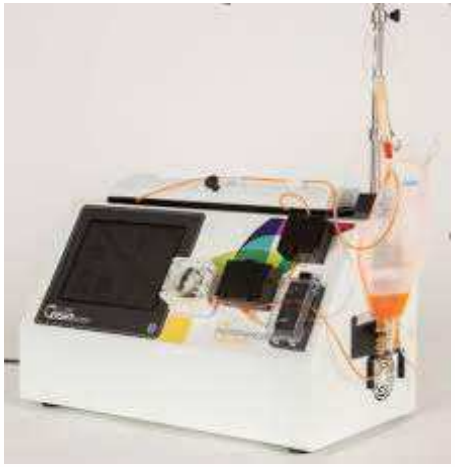
ACD = Acid Citrate Dextrose, QC = Quality control

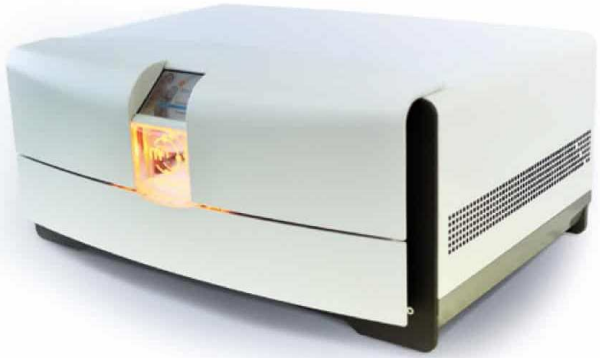
Arora S, Setia R. Extracorporeal photopheresis: Review of technical aspects. Asian J Transfus Sci 2017;11:81-6

ECP : PHOTO-INACTIVATION of MNCs

Performed by automated devices

- **photoreactive substance**: 8-methoxypsoralen (8-MOP) added to cellular collection
- **Activatation of 8-MOP**: by ultraviolet A irradiation (wavelenght 350- 415 nm)
- **Effect** : cross-linking of DNA strands triggering an apoptotic cascade





ECP : Apoptosis of mononuclear cells

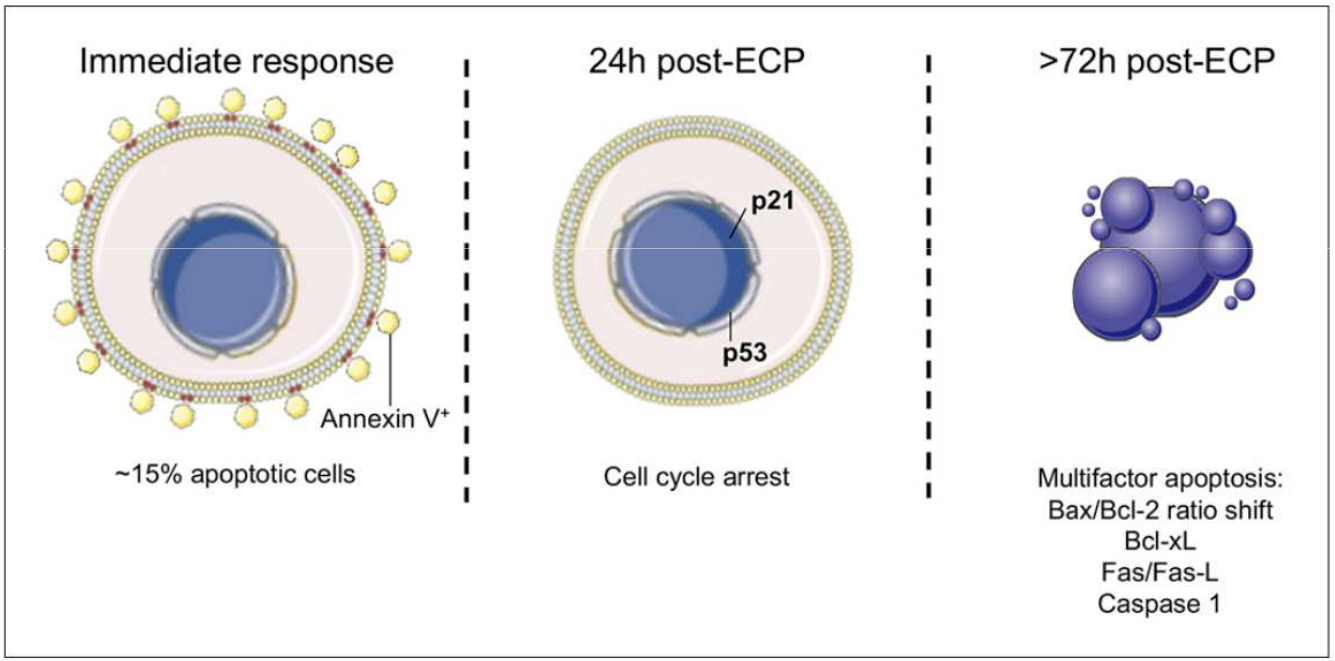


Fig. 1. Cell cycle arrest and commitment to apoptosis of ECP-exposed cells. Upon exposure to ECP cells that suffer extensive DNA damage, fail to repair it or bear severe mitochondrial alterations initiate a gradual process of apoptosis. Severely affected cells have an immediate flip-flow of phosphatidylserine, others halt cell cycle via activation of p21 and p53, and apoptotic bodies appear as early as 72 h after treatment as a result of activation of both intrinsic and extrinsic apoptosis pathways.

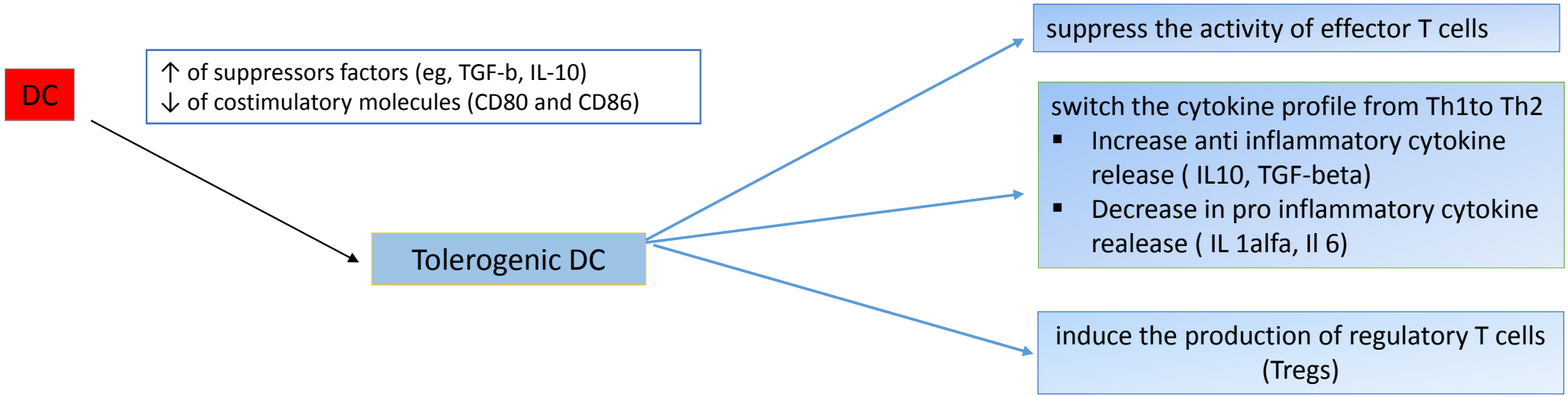
The susceptibility to ECP-induced apoptosis varies from cell type to cell type:

- **B cells and NK cells**: over 70% of apoptotic cells after 24 h (increasing >90% after 48 h).
- **T lymphocytes**: highly susceptible up to 90% after 48 h.
- **Monocytes**: apoptosis above 90% 72 h after treatment; those who survive are able to differentiate into dendritic cells (DC)
- **T-regs**: apoptosis levels below 30% at 24 h and levels of 30–65% 48 h after treatment

P.A. Vieyra-Garcia et al Transfus Med Hemother 2020;47:226–234

ECP - IMMUNOTOLERANCE

- ECP induces apoptosis on leukocytes; when these apoptotic cells return to patient, they are cleared by antigen presenting cells (DCs).



Marc Xipell and Alícia Molina-Andújar, Immunogenic and immunotolerogenic effects of extracorporeal photopheresis in high immunological risk kidney recipients. A single center case series; J Clin Apher. 2022;37:197–205.

ECP- side effects

- **During collection:**
  - **Systemic hypocalcemia** requiring intravenous calcium replacement;
  - **Hypotension**;
  - **Catheter related beeding or infection;**
- **Related to 8 MOPP exposure**
  - (increased urinary output, metallic taste, and sparkly bits in the eyes);
- **At ECP products infusion**:
  - **mild fever, tiredness**
  - **hematuria** (due to reinfusion of red blood cell
- **Long –term side effects**
  - Hypochromic anemia
  - photosensitivisation

ECP IN TRANSPLANT SCENARIO
(according to the 2023 American Society for Apheresis [ASFA] guidelines)

ECP is currently indicated as an immunomodulatory treatment for many organ transplants, but not in KT.

1. **Heart transplantation :**
   - **cellular/recurrent graft rejection**(ASFA category II, grade 1B),
   - **rejection prophylaxis** (ASFA category II, grade 2A).
2. **Lung transplantation:**
   - early bronchiolitis obliterans syndrome (BOS) (, category II, grade 1C) stabilization of lung function
   - persistent acute rejection.
3. **Liver transplantation** (ASFA category III, grade 2B)
4. **Allogeneic stem cells transplantation**
   - **steroid-refractory acute and chronic GVHD** (ASFA category II; grade 1C and 1B, respectively), with an overall response rate reported of 52% to 100% depending on the affected organ

ECP in Kidney Tranplantation

Study	Type of study	N° pts	Indication for ECP	ECP	Results
Jonathan T. Wolfe et al. (1996)	Case report	1 pt	severe acute rejection, predominately of a vascular nature (ISN grade 3)	four ECP over an 8-day period	improved blood flow and function of the allograft
Meg J. Jardine et al. (2009)	Prospective case series	10 pts	rejection unresponsive to current therapy	weekly ECP (total of 4), then fortnightly ECP; total range was 5-12 ECP for more than 5–20 weeks	Resistant rejection resolved in all patients (stabilization of previously unstable renal function)
Fernández Granados S, et al. (2020)	Retrospective descriptive study	8 pts	**contraindication to ST** (n = 4) due to concomitant infection (50%), **unresponsiveness** (n = 4) to the ISS treatment	two consecutive sessions a week for five weeks, with additional sessions depending on the progress on completing the first round	Improvement in graft function in pts with ACR (n = 4). Late ACR unable to complete the initial regimen. None of the grafts with a humoral component showed improvement. One CAHR suffered loss of the graft.

ECP in Kidney Tranplantation

Study	Type of study	N° pts	Indication for ECP	ECP	Results
Xipell M, et al. (2022)	single center case series	4 pts	rejection of kidney graft refractory to treatment + concomitant infection	Mean n° of sessions: 14.75 Regimen not specified	stabilization of renal function in 3/4 pts (2 remained stable after EOT, 1 worsened again)
M. Tamain et al. (2019)	multicentre retrospective study	33 pts • 23 acutes AMRs, • 2 chronic AMRs • 8 acute cellular rejections (ACRs)	resistance or contraindication to ST (concomitant infections or cancers)	2/week in 27 pts 1/week in 6 pts for one month. Manteninance: 1/month. Median of 12.5 [3-60] ECP sessions over 3.5 months [0.5-67.5].	Month 12 post-ECP: 11 pts stabilization of kidney function with a graft survival rate of 61%

ECP in Kidney Tranplantation

indication to ECP:

- acute/chronic cellular rejection , moderate AMR
- contraindication to conventional ISS therapy (active or high-risk of infection or concomitant cancer**)**
- refractory to conventional treatment

Predictive factors for response

- Serum creatinine level < 4.5 mg/dl
- Early ECP initiation

M. Tamain et al. (2019) Extracorporeal photopheresis for the treatment of graft rejection in 33 adult Kidney transplant recipients, TAS 2019, 58:515-524

F. Granados S et al. Fotoféresis extracorpórea y trasplante renal. Nefrologia. 2020;40:687–689.

M. Xipell et al , Immunogenic and immunotolerogenic effects of extracorporeal photopheresis in high immunological risk kidney recipients. A single center case series; J Clin Apher. 2022;37:197–205.

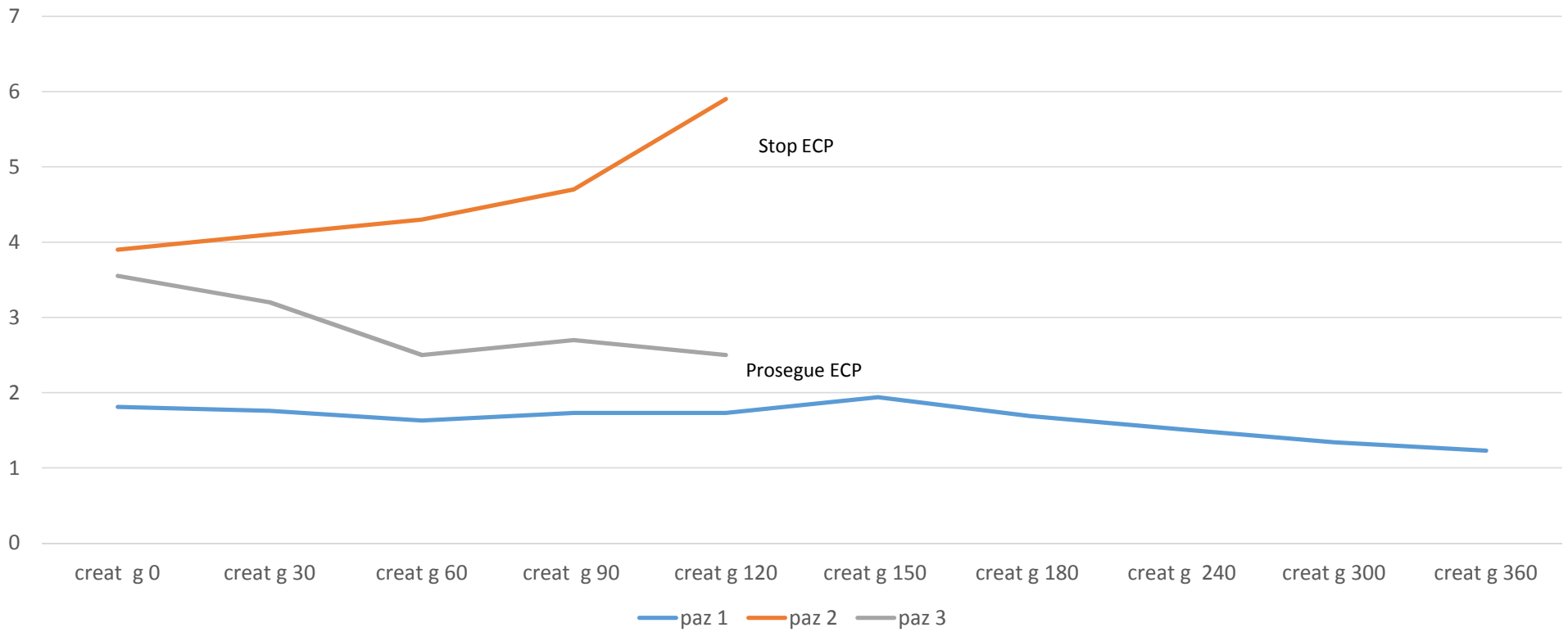
ECP nel trapianto renale

Pz	Età	Diagnosi	Data trap renale	comorbidità	Istologia alla Bio renale		DSA	Terapia effettuata
BMG	46	Glomerulonefrite extracapillare (1995)	I° 05/06/1998 **II° 08/04/2014**	BKV Baselioma cutaneo	10/09/2020	Rigetto cellulare cronico	ND	MP 250 mg x 3 gg
SF	50	Glomerulonefrite mesangiale	I° 1993 (da vivente) **II° 10/01/2018** (PRA 85%)	Baselioma cutaneo	29/11/2021	Rigetto umorale cronico attivo	Ab anti HLA di classe II (DQA)	-
N E	71	Rene policistico	**I° 14/04/2022** (da vivente)	Cardiomiopatia ischemica Steatosi epatica (pregresso contatto HBV)	22/4/2022	Rigetto acuto vascolare con associate alterazioni glomerulitiche acute (CMR II B , BANFF)	Classe I B14 (MFI 1940) **Classe II DR53 (MFI 33600)**	Tymoglobuline PEX (8 tot) IGG ev specifiche

ECP nel trapianto renale

Pz	Indicazione a ECP	Data inizio ECP	Tempo Rigetto-start ECP	Schema trattamento	Numero Procedure totali	Volemie trattate /proc	Volume cellulare raccolto	Dose MNC /kg infuse
BMG	peggioramento funzione renale Comorbidità	5/10/2020	1 mese	1 proc / 2 sett x 4 1 proc/3 sett x4 1 proc/mese	28	1,7 (5400 ml)	159 ml (130-183)	0.7 x 10^8 /kg
SF	Peggioramento funzione renale Pz iperimmune	28/2/2022	3 mesi	1 proc / 2 sett x 4 1 proc/3-4 sett x5	9	1,7 (6000 Ml)	158 ml (137-179)	0.5 x 10^8 /kg (0.4-0.5)
N E	Peggioramento funzione renale in recente AMR (già trattata con PEX, Ig Ev	04/1/2023	-	1 proc / 2 sett x 4 1 proc/3 sett x3 1 proc/mese	9	1,7 (7450 ml)	230 ml (173-245)	0,3 x 10^8 /kg (0,27-0,4)

Valutazione risposta ECP: andamento creatinina



ECP nel trapianto renale

I risultati ottenuti (stabilizzazione della funzionalità renale in 2/3 pz) rendono probabile l'arruolamento di nuovi pazienti.

Aree di miglioramento:

- miglior definizione dei criteri di selezione dei pazienti da avviare a ECP
- Valutazione di parametri biologici di risposta attraverso il monitoraggio delle cellule T_ regolatorie

Conclusioni: un ringraziamento a tutti!

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