Apheresis in Kidney Transplantation

Is There Still a Place in the Era of New Therapies?

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Disclosures

I have nothing to disclose
regarding this presentation.

Presentation carbon footprint ~ 2.86 kg CO2e, (98% derived from train travel (Grenoble-Paris))


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Congrès Médical 2056 - Néphrologie & Transplantation

Outline

1. **Antibody-Mediated Rejection (ABMR)** *Plasmapheresis, Immunoadsorption : what evidence in 2026?*
2. **Desensitization in ABO & HLA incompatible KTx** *The backbone of pre-transplant preparation*
3. **Recurrence of Nephropathy Post-KTx** *FSGS, MPGN : when apheresis changes the game*
4. **The Big Question** *Anti-CD38, bispecifics, Imlifidase, CAR-T … will they replace apheresis?*

Apheresis: Mechanism of Action in Antibody-Mediated Diseases

Plasmapheresis (PP)	Double Filtration (DFPP)	Immunoadsorption (IA)
Non-selective removal of all plasma proteins	**Selective for large molecules**	**Specific or semi-specific antibody** removal Protein A, anti-IgG, or antigen columns

Key Antibody Targets in Kidney Transplantation:

- Anti-HLA DSA
- ABO isoagglutinins
- Anti-nephrin (FSGS)
- ANCA
- Anti-Factor H / I (aHUS)

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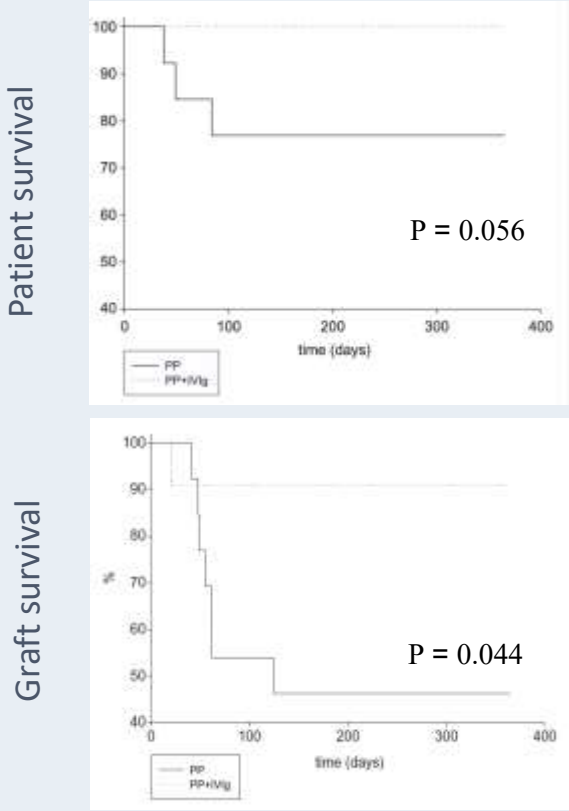
Antibody-Mediated Rejection (AMR)

Evidence for apheresis and its limits in 2026

ABMR Treatment: Historical Evidence for Plasmapheresis

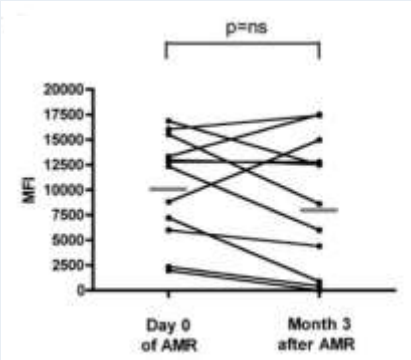
- **Soulillou et al.** 1983 : First reports of PE in acute humoral rejection (no effect)
- **Allen et al.** 1983 : Controlled trial: PE in acute renal allograft rejection (no effect) (N=13 & 14)
- **Böhmig et al.** 2007 : RCT (n=10): Immunoadsorption in severe C4d+ acute rejection (IA): ↗graft survival (N=5 & 5)
- **Rocha et al.** 2003 : PE + IVIg: similar outcomes on graft survival in early AMR versus TCMR (N=16)
- **Slatinska et al**. 2009 : PP ± IVIg: improved patient & graft survival (N=13 & 11)

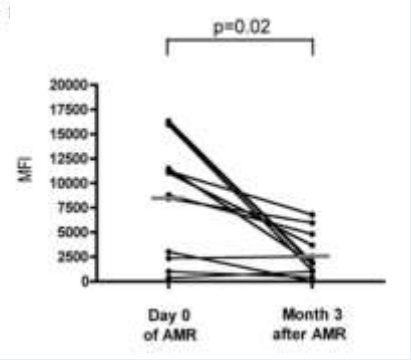


Slatinska et al. Ther Apher Dial 2009

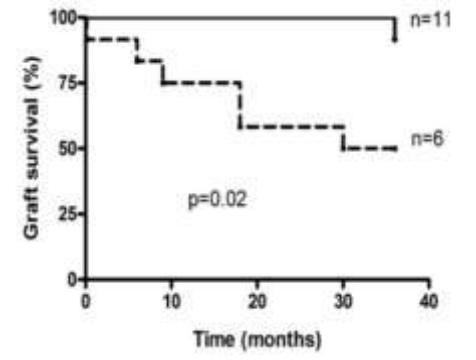
AMR: **IVIg Alone** vs **PP + IVIg + Rituximab** (retrospective, monocentric)

n=12 patients	n=12 patients
IVIg **2000-2003** 2g/kg × 4 Every 3 weeks	**IVIg +** **PE + Rituximab** **2004-2005** PP/d IVIg 2g/kg × 4 RTX 375 mg/m² × 2





Immunodominant DSA



Graft survival

Lefaucheur C et al. Am J Transplant 2009;9:1099-1107

RITUX-ERAH: Prospective RCT (Rituximab)

40 patients with acute ABMR : PLEX + IVIg + Steroids ± Rituximab 375 mg/m²

	Placebo	+ Rituximab	
Graft survival at 1 / 7 years	94.7% / 55%	94.7% / 44%	NS
Primary endpoint (graft loss Or loss of function <30%)	52.6%	57.9%	NS
DSA MFI <2000 at M12	40%	76.5%	p<0.04 ✓

Key message: Rituximab significantly reduced DSA levels at 1 year but did NOT improve graft survival or function

Sautenet B et al. Transplantation 2015. Bailly et al. Transplant International 2020

Imlifidase vs Plasmapheresis in AMR

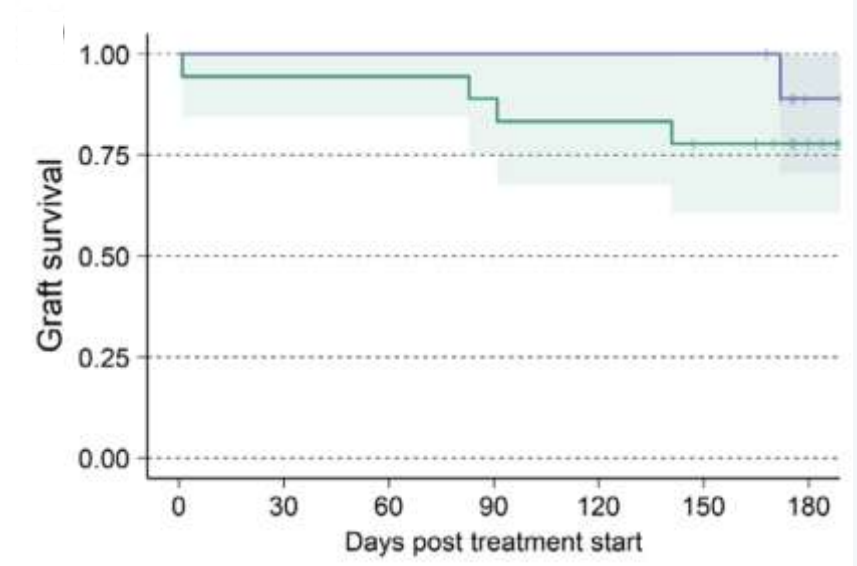
30 patients, 14 centers, 6-months open-label RCT: Imlifidase (n=18) vs PLEX (n=10)

Imlifidase

- DSA reduction at **day 5**: 97%
- Achieves non-complement-fixing levels
- DSA rebound days 6-12
- 4/18 graft losses at 6 months
- KM graft survival: 78%

Plasmapheresis

- DSA reduction at **day 5**: 42%
- Fails to reach non-complement-fixing levels
- More sustained DSA reduction
- 1/10 graft losses at 6 months
- KM graft survival: 89%



eGFR slightly higher in PLEX

Halleck F et al. Clin Transplant 2024;38:e15383

ASFA Guidelines: Apheresis in ABMR (2023)

Category I: first-line therapy
AMR in kidney transplantation
1B
Strong recommendation, moderate evidence

Standard protocol:

- PP or IA: 5-10 sessions
- IVIg 100mg/kg after each session
- ± Rituximab
- Steroids

Transplantation, kidney, ABO compatible	Antibody-mediated rejection	TPE/IA	I	1B	257
	Desensitization/prophylaxis, living donor	TPE/IA	I	1B	

ASFA 2023 Guidelines J Clin Apher

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Desensitization
ABO & HLA Incompatible KTx

Apheresis as the cornerstone of pre-transplant preparation
For which benefit ?

ABO-Incompatible KTx: Apheresis is the gold-standard (so far)

~30%
Of potential living donors are ABO-incompatible

32%
expanded access to transplantation

≤ 1:8
target isoagglutinin titer pre-KTx

Accommodation post-KTx reduces most of humoral rejection risk

Why rituximab alone is not enough:

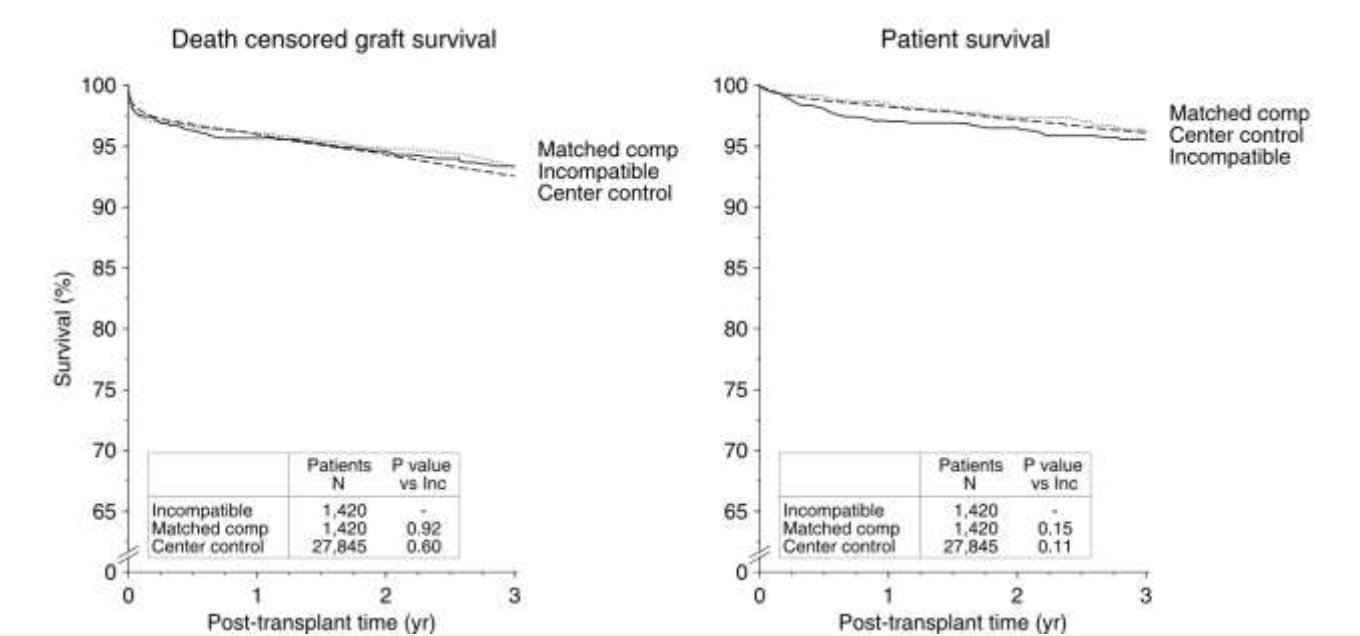
- Habicht et al. (NDT 2011): Rituximab alone reduced isoagglutinin titers, but only apheresis reliably achieves ≤1:8 threshold required for safe transplantation
- Apheresis allows to achieves rapid isoagglutinin clearance before transplant with good outcomes

Transplantation, kidney, ABO incompatible	Desensitization, living donor	TPE/IA	I	1B	259
	Antibody mediated rejection	TPE/IA	II	1B	

Habicht A et al. NDT 2011;26:4124-4131

ABOi KTx: Outcomes vs ABO-Compatible Transplantation

- ABOi : **1 420 patients**
- Matched ABOc : 1 420 patient
- Control cohort : 27 845 patients

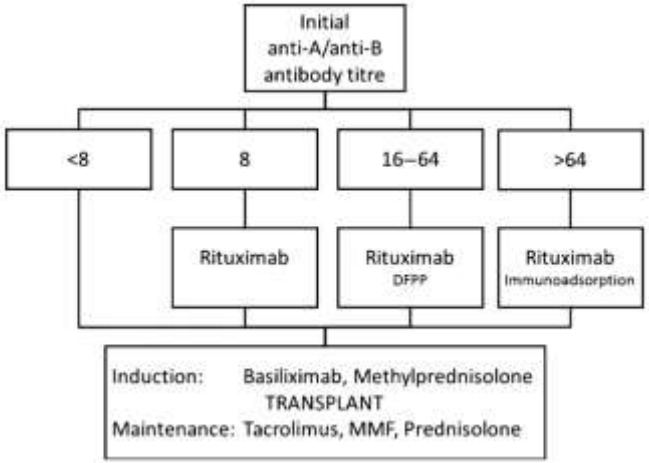


ABO antibody reduction by column **adsorption** was associated with similar death-censored graft survival to **plasmapheresis**

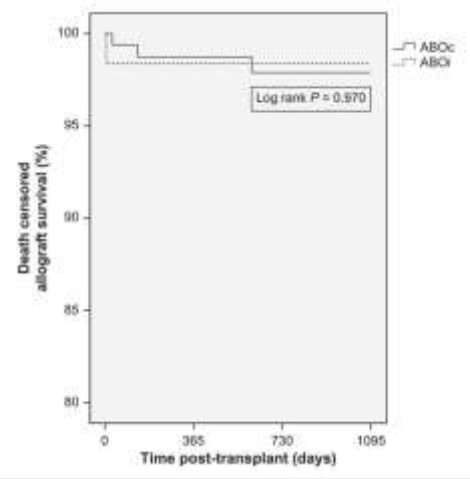
Opelz et al. Transplantation 2015, Feb;99(2):400-4.

Tailored Desensitization According to Isoagglutinin Titer

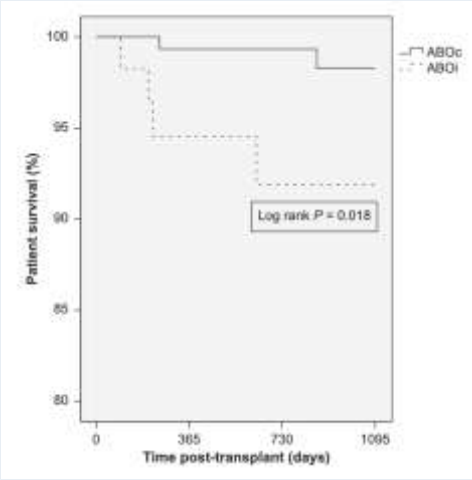
Modified protocol according to ABGA titer:



Nicholas R Barnett et al, Transplant International, 2014.



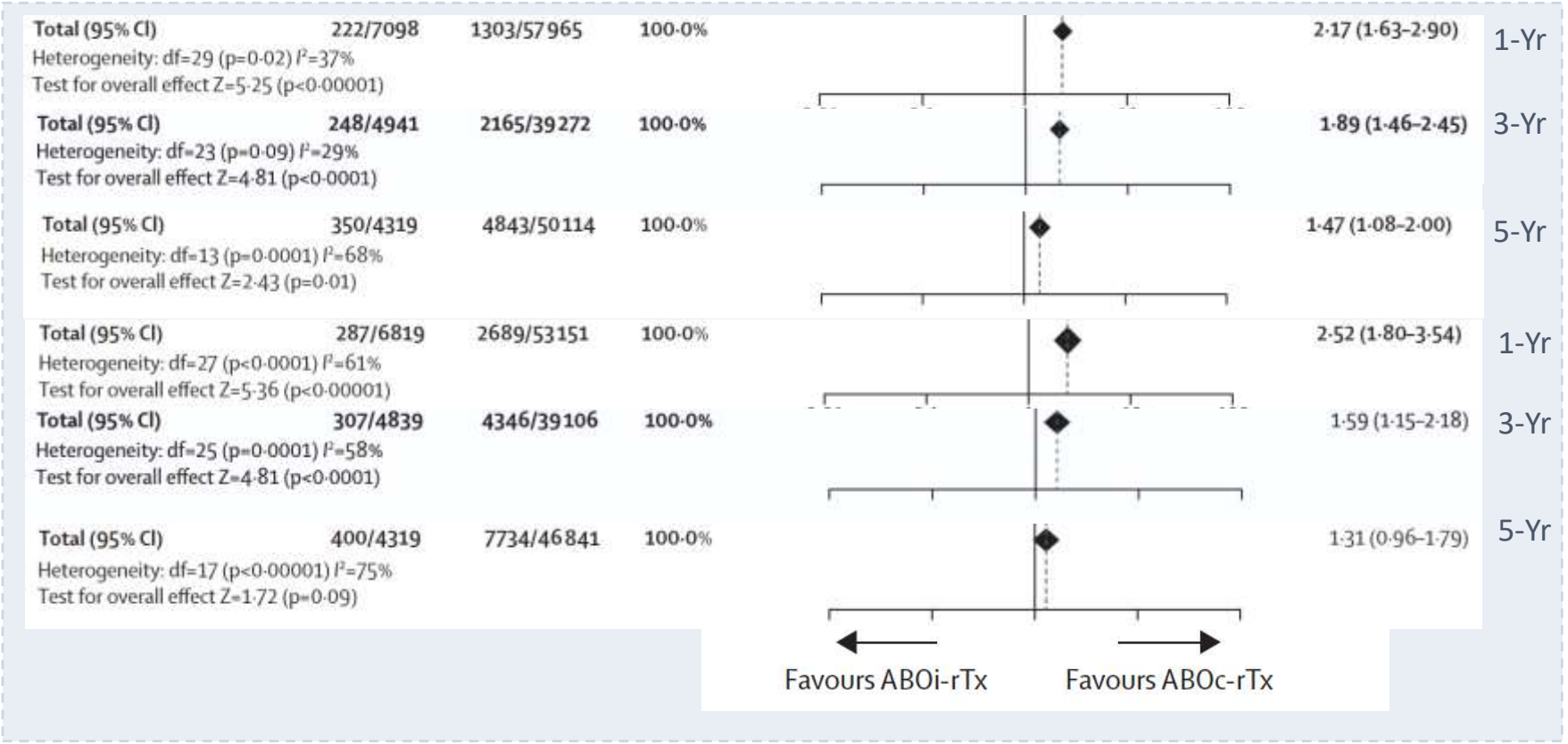
Death censored graft survival



Patient survival

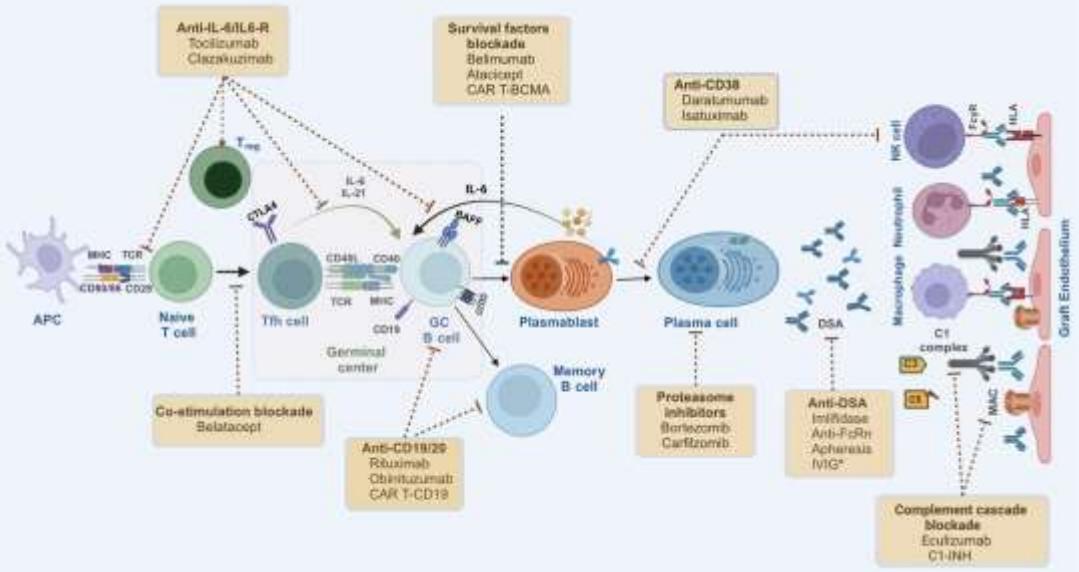
- **High titer** (≥1:1024): extended IA sessions until ≤1:8 : good results
- Low/moderate titer: standard 4–6 sessions of specific IA or DFPP : comparable outcomes

Clinical Outcomes After ABOi Renal Transplantation: Metaanalysis



Scurt FG, Ewert L, Mertens PR, Haller H, Schmidt BMW, Chatzikyrkou C | Altindal M et al. Clin Kidney J 2025

HLA-Incompatible KTx: Desensitization Strategies



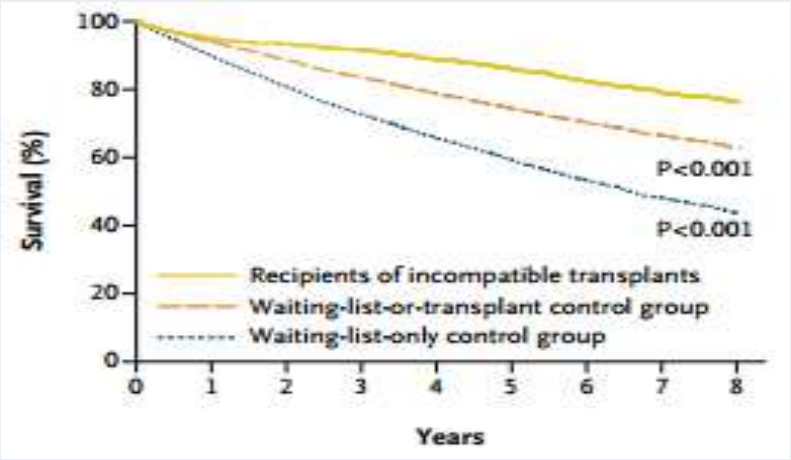
Current stepwise approaches:

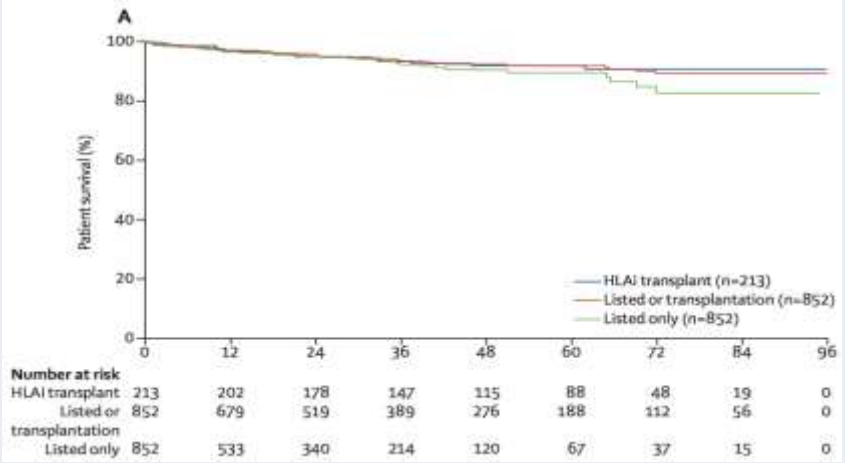
PP / IA	Pre-tx DSA reduction
+ IVIg	Suppress antibody rebound
+ RTX	B-cell depletion
± Eculi-zumab	Complement inhibition

Individualized = based on DSA MFI & crossmatch

Altindal M et al. Clin Kidney J 2025

Survival Benefit with KTx from HLA-Incompatible Live Donors





USA

22 centers
1025 HLAi
5125 matched patients

UK

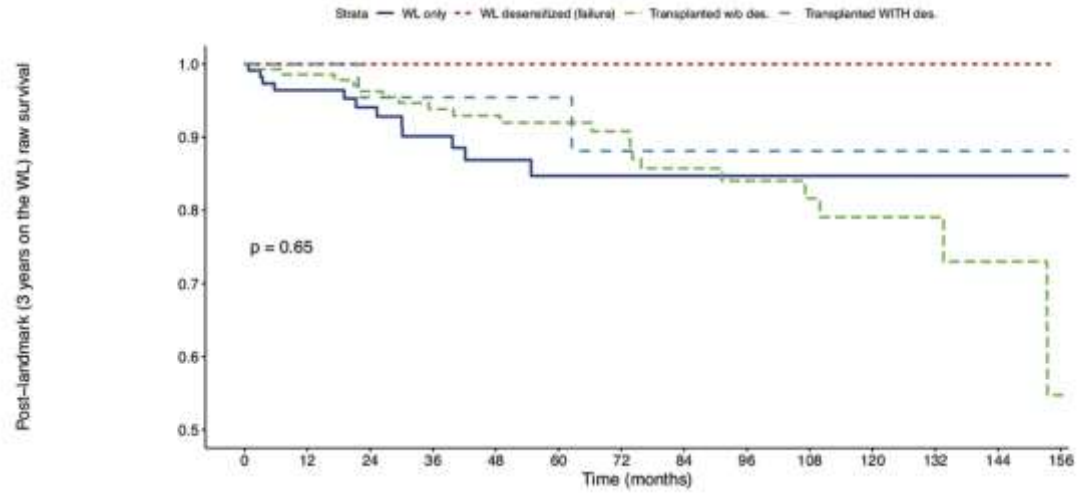
213 HLAi
852 matched patients

Living donors

Orandi BJ et al. N Engl J Med 2016 | Manook M et al. Lancet 2017

Survival Benefit with KTx from HLA-Incompatible - Grenoble experience

- **326 highly sensitized** waitlisted patients (26 desensitized, 30 transplanted)
- **Patient Survival**: No difference between desensitized KT, non-desensitized KT, and waitlisted patients (HR = 0.48, p = 0.22)
- **Death-Censored Graft Survival**: Similar
- **1-Year Graft Function**: Equal mean eGFR (53.3 vs. 53.6 mL/min/1.73m², p = 0.95).



Noble *et al* Kidney Int Rep, 2021

Apheresis Efficacy & Tolerance in HLA-Incompatible KTx

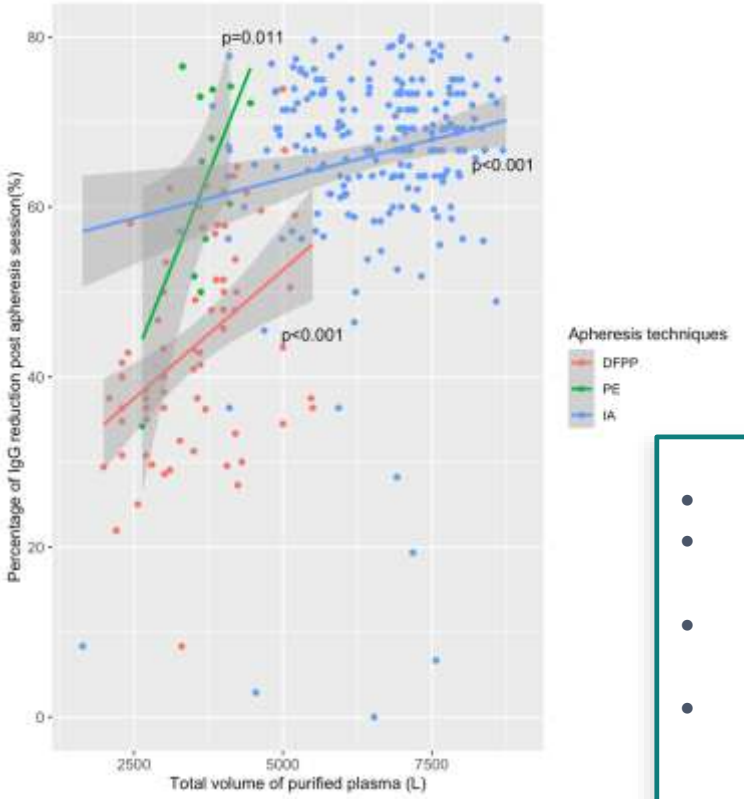


Table 5. Biological parameters according to apheresis techniques.

	DFPP (*N* = 107)	PE (*N* = 54)	IA (*N* = 720)	Total (*N* = 881)	*p*-Value
Pre-post IgA evolution (%) Median [IQ]	−55 (−45; −63)	−48 (−1; −71)	−14 (−7; −21)	−17 (−8; −29)	<0.01
Pre-post IgG evolution (%) Median [IQ]	−40 (−31; −50)	−61 (−46; −73)	−60 (−33; −70)	−56 (−33; −69)	<0.01
Pre-post IgM evolution (%) Median [IQ]	−37 (0; −58)	−51 (60; −75)	−17 (0; −54)	−17 (0; −57)	0.10
Pre-post Alb evolution (%) Median [IQ]	1 (14; 2)	10 (14; −3)	9 (14; −1)	9 (15; 0)	0.73
Pre-post fibrinogen evolution (%) Median [IQ]	−61 (−56; −69)	−33 (−29; −64)	−43 (−22; −57)	−47 (23; −60)	<0.01
Pre-post hemoglobin evolution (%) Median [IQ]	15 (22; −8)	2 (10; −2)	2 (9; −2)	3 (11; −2)	<0.01
Pre-post leukocytes Evolution (%) Median [IQ]	65 (96; 33)	22 (60; 5)	4 (18; 8)	8 (27; 6)	<0.01
Pre-post platelet evolution (%) Median [IQ]	7 (−1; 17)	14 (2; 21)	12 (3; 21)	12 (2; 21)	0.01

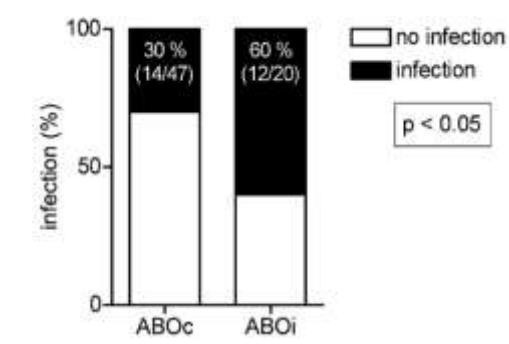
severe adverse events occurred in 17 sessions (1.9%)

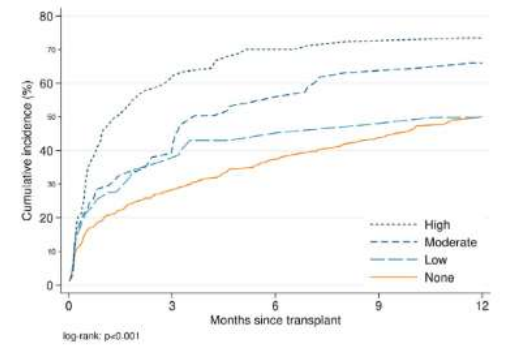
- 107 DFPP, 54 PE, 720 IA.
- Volume of treated plasma significantly associated with IgG reduction post-apheresis (**IA requires a greater volume**)
- DFPP less efficient on class II

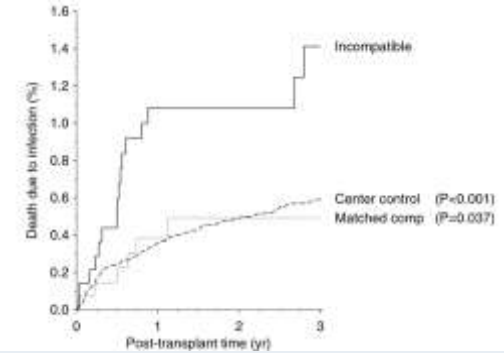
- **Monet filter** (cascade IA): significantly higher reduction of IgG, IgM and IgA vs IA alone

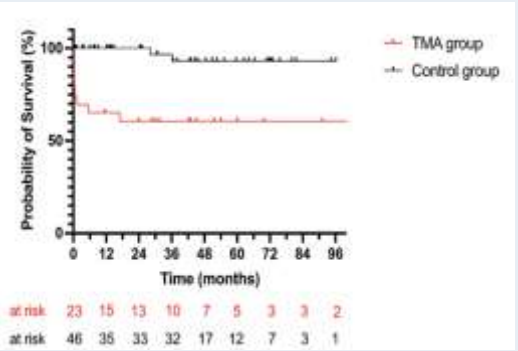
Noble J, et al. J Clin Med 2021

Risks associated with PE in desensitized patients: infections, TMA, death

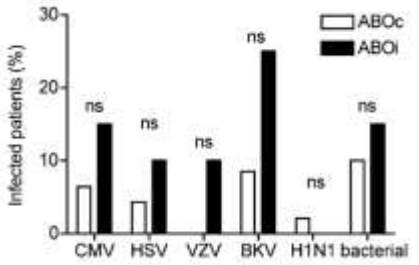








Correlation between intensity of apheresis and infectious risk



- Intensity of apheresis correlates directly with infectious risk
- Prophylaxis: cotrimoxazole + penicillin V
- Anti-meningococcal (Nimenrix + Bexsero) + anti-pneumococcal (Prevenar 13)
- IVIg 0.1g/kg if IgG < 2g/L post-session

Habicht A et al. NDT 2011 | Avery, R. K. et al. AJT 2020; | Opelz et al. Transplantation 2015 | Bertrand et al. Kidney Int Rep 2025

3

Post-KTx Nephropathy Recurrence

FSGS, MPGN, MN..
may apheresis improve graft survival ?

FSGS Recurrence Post-KTx: Epidemiology

32%
FSGS recurrence rate

39%
graft loss in recurrers
median 5 years

81%
treated with
PP + Rituximab

57%
partial or complete
remission with treatment

Risk factors for recurrence:

- **Older age** at onset of native kidney disease (HR 1.37/decade), **lower BMI**, prior native **nephrectomy** (HR 2.76)
- Circulating permeability factor: **anti-nephrin** autoantibodies emerging as key mediator
- Partial or complete remission significantly associated with better graft survival

Uffing A et al. Clin J Am Soc Nephrol 2020

FSGS Recurrence: PE + Rituximab

- PP removes **circulating permeability factor** (anti-nephrin Ab?)
- Remission rates higher with combined PP + RTX than RTX alone

- **Prophylactic PP** pre-KTx in high-risk patients ?
- **Response to PP** predicts graft outcome

Key References

Dantal J et al. N Engl J Med 1994 **(N=8)**

Deegens JK et al. Transpl Int 2004 **(N=13 vs 10)**
Graft survival 85% and 30%, respectively, at 5 years (P=0.02)

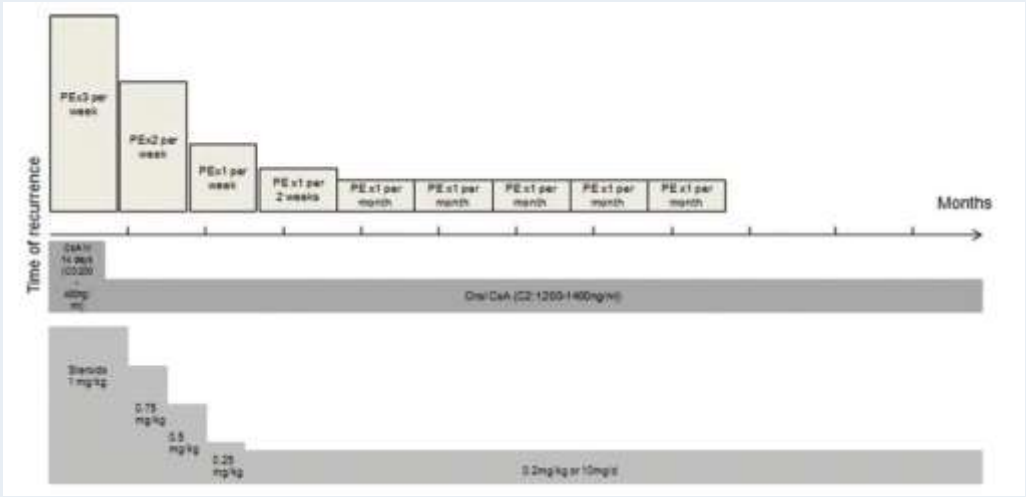
Hickson LJ et al. Transplantation 2009 **(N=30)**
pediatric cohort

Garrouste et al. Transplantation 2017 **(N=19)**

Canaud G et al. Am J Transplant 2009 **(N=10 vs 10)**

Uffing A et al. CJASN 2020 **(N=176)**

FSGS Recurrence: PE + Immunosuppression (open label, non-randomized)



- FSGS recurrence
- 10 patients with Steroids + CsA + PE
- 19 controls

- Complete remission **90% vs 27%** controls (p<0.001)
- 1 patient PE-dependant
- **Early initiation critical**
- 1-year biopsies did not show progressive interstitial fibrosis

Canaud G et al. Am J Transplant 2009

FSGS Recurrence: PP + Rituximab

Table 3. Immunosuppressive treatment modalities for recurrent FSGS and corresponding outcomes

Treatment	No Remission	Partial Remission	Complete Remission	Total
Plasmapheresis	7 (28)	11 (44)	7 (28)	25
Plasmapheresis + rituximab	16 (53)	9 (30)	5 (17)	30
Immunoadsorption[a]	2 (67)	1 (33)		3
Rituximab only		1 (50)	1 (50)	2
Plasmapheresis + cyclophosphamide	1 (100)			1
Steroids only	5 (83)	1 (17)		6
Cyclosporine[b]	2 (67)	1 (33)		3
No treatment	5 (100)			5
Total	38 (51)	24 (32)	13 (17)	75

[a]Two patients dependent on immunoadsorption had received plasmapheresis and rituximab treatment without remission, one patient had received only rituximab and immunoadsorption.
[b]Patients were switched from oral tacrolimus to oral cyclosporine. Treatment was not given intravenously.

- **Graft survival higher with combined PP + RTX** than **RTX alone**

Uffing A et al. CJASN 2020

MPGN Recurrence Post-KTx: retrospective & multicentric

- 220 KTx with biopsy proven MPGN
- 37 % of kidney failure
- 25% of recurrence

Variable	Univariate analysis HR (95% CI)	P-value
Treatment with rituximab for recurrence		.16
No	1.00 (reference)	
Yes	0.47 (0.17–1.34)	
Treatment with plasma exchange for recurrence		.16
No	1.00 (reference)	
Yes	2.18 (0.73–6.52)	
Treatment with MMF dose increase for recurrence		.62
No	1.00 (reference)	
Yes	0.72 (0.20–2.65)	
Treatment with eculizumab for recurrence		.47
No	1.00 (reference)	
Yes	0.61 (0.16–2.36)	

- IC-MPGN: PP removes immune complexes and complement factors
- Complement-mediated: eculizumab cornerstone
- IA + Monet filter: removes complement more efficiently than IA alone
- Role of PP largely anecdotal : no RCT available

Caravaca-Fontán F et al. NDT 2023

Membranous Nephropathy Recurrence ?

Hypothesized Mechanisms of Apheresis Efficacy

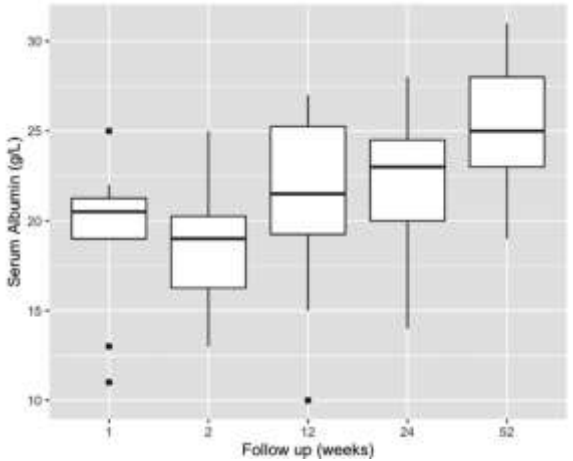
1 **Anti-PLA2R antibody removal**

2 **Complement & cytokine clearance**

Supported by case report efficacy in seronegative MN (Ma et al. Semin Nephrol 2013)

Key Clinical Evidence

12 patients, anti-PLA2R >170 U/mL, 5 daily IA sessions
Albumin ↑ significantly ($p<0.001$) but no change in proteinuria
Antibody rebound on stopping IA



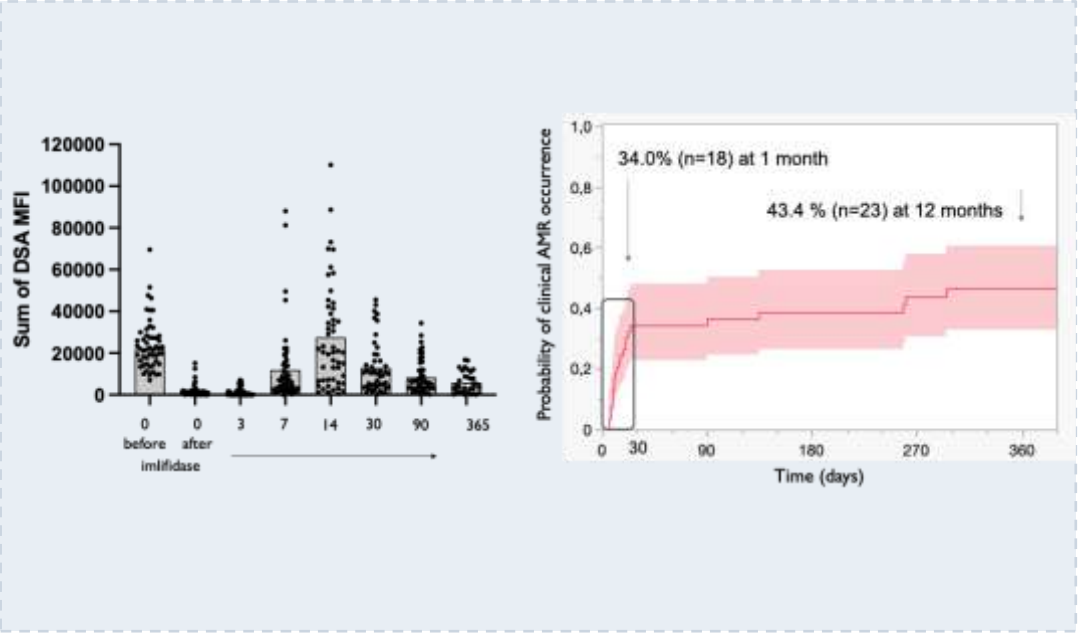
Hamilton The PRISM Trial JCA 2018

Apheresis in MN: evidence limited to case series: no RCT
Need for combined B-cell targeted therapy (RTX, Obinutuzumab) ?

The Big Question:
Do New Therapies (will) replace apheresis?

Anti-CD38 | Bispecific antibodies | Imlifidase

IgG Endopeptidase (Imlifidase) in Highly Sensitized Patients



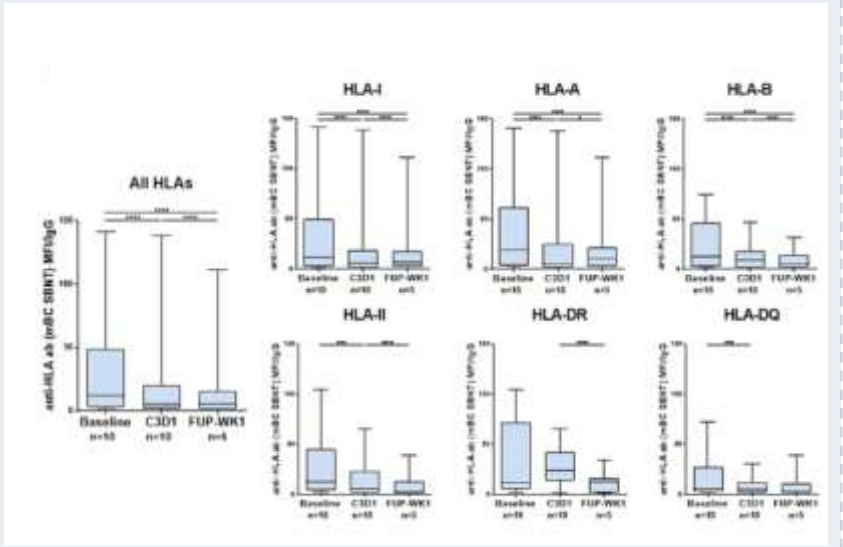
- Kjellman AJT 2021 : 39 patients
- AMR–: graft survival 93% | patient survival 85% at 3 years
- AMR+: graft survival 77% | patient survival 94% at 3 years

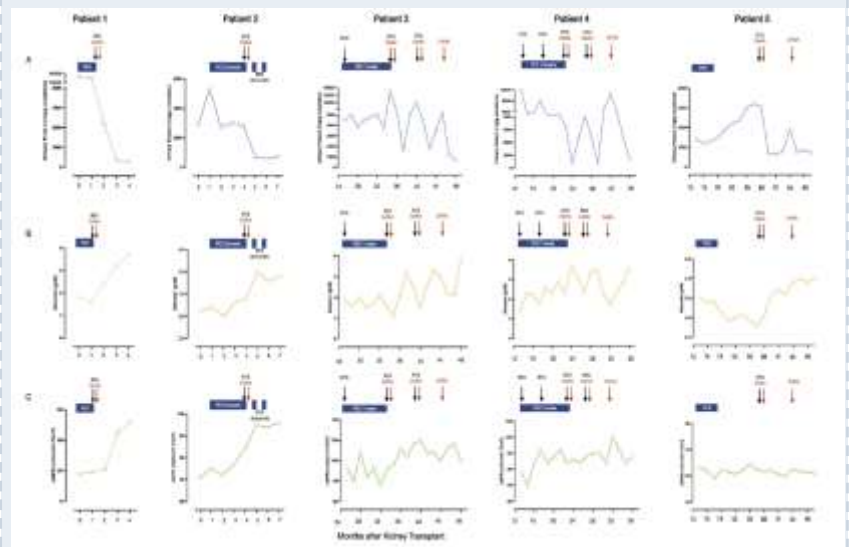
- ISKIA:
- Patient survival : 95.7% at 12 months
- Graft survival : 97.8% art 12 months

Antibody rebound D6–12 : maintenance IS essential; DSA recurrence remains the major challenge

Original data from the ISKIA French registry, Kjellman AJT 2021

Anti-CD38 (Daratumumab) in Kidney Transplantation



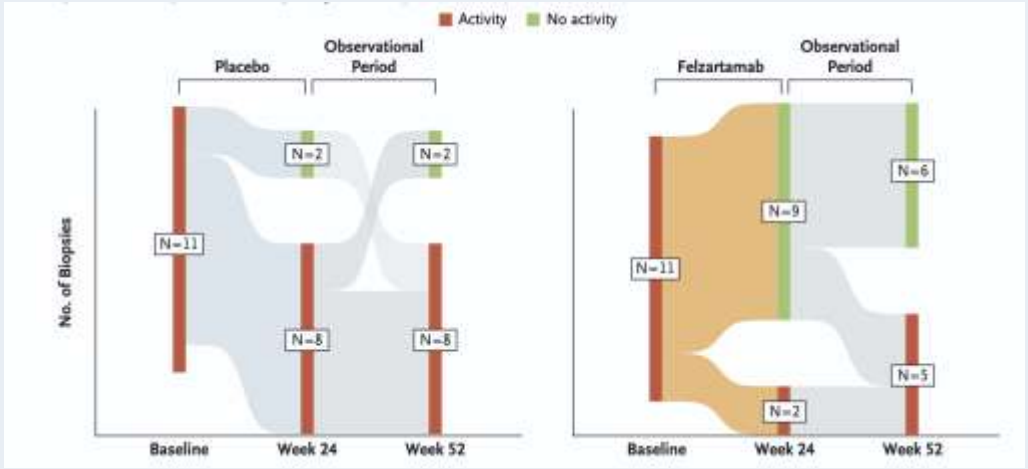


Desensitization / AMR

FSGS Recurrence: Sequential Rituximab + Daratumumab

Torija A al. Am J Transplant 2024; Angeletti A,. Am J Transplant 2024

Felzartamab (Anti-CD38) in ABMR : Phase 2 RCT

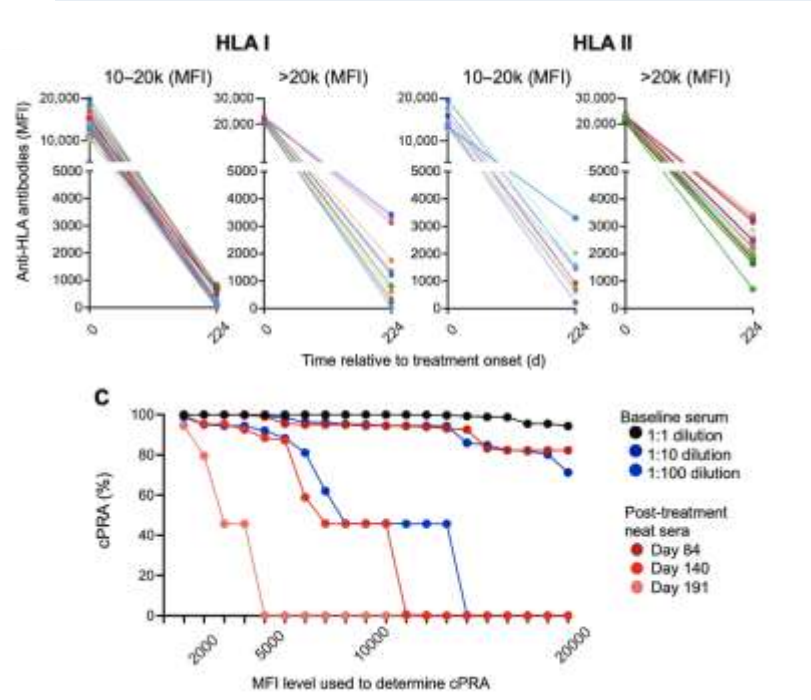


- **Phase 2 RCT** : felzartamab vs placebo in active ABMR
- Significant **reduction of Banff ABMR scores** at 24 weeks
- Molecular phenotype improvement (IFTA, inflammation)
- DSA reduction
- Nat Med 2025: biopsy-level molecular effect confirmed

First RCT data for anti-CD38 in ABMR : promising, but combination with apheresis not yet defined

Mayer KA et al. NEJM 2024;391(2):122-132 | Diebold M et al. Nat Med 2025

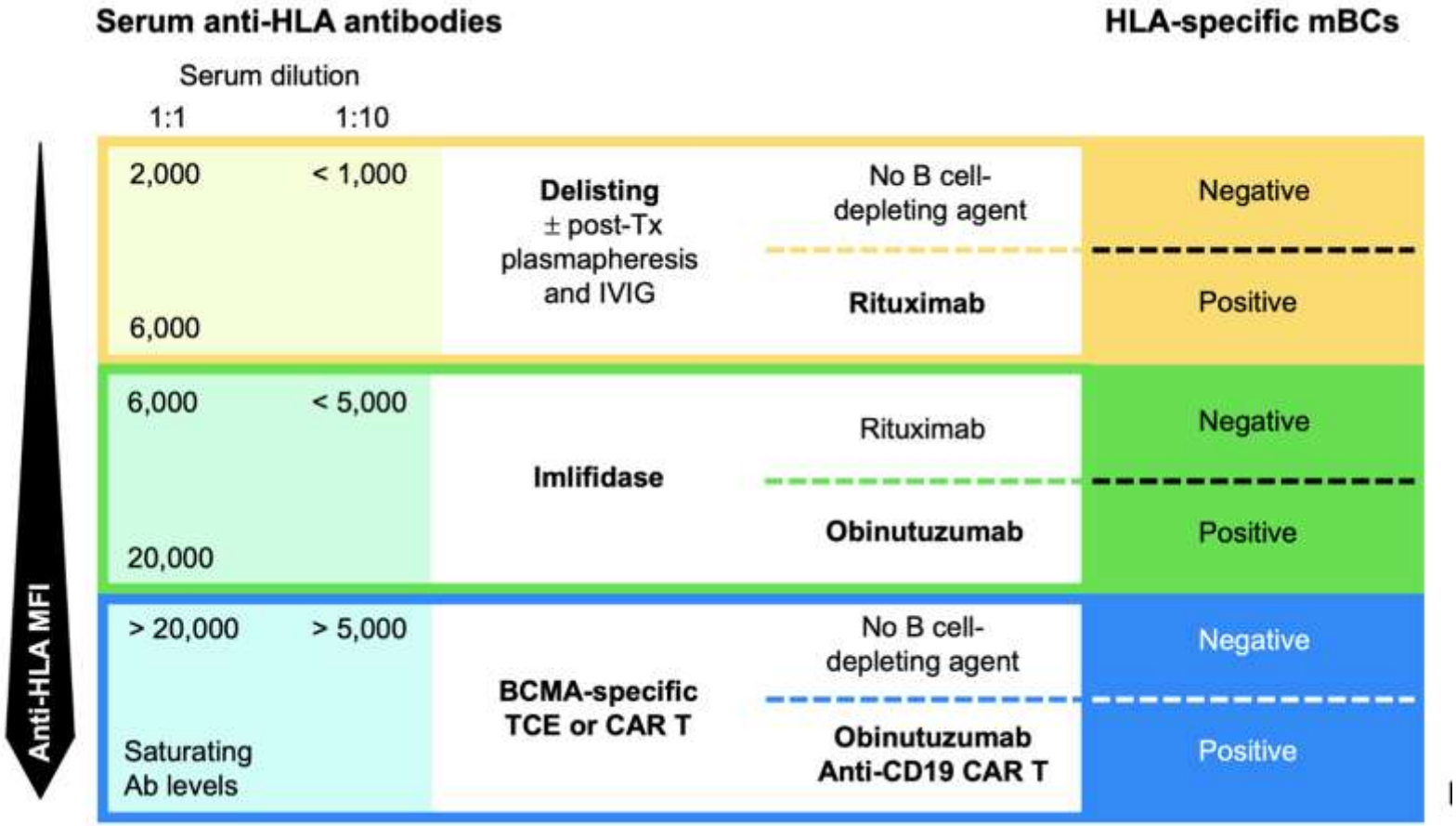
BCMA T-cell Engager + B-cell Depletion for Refractory HLA Sensitization



- Combination: **BCMA T-cell engager + anti-CD20 B-cell depletion**
- First clinical data in **refractory HLA-sensitized** transplant candidates
- Significant DSA reduction : enables access to transplantation in previously untransplantable patients

Proof of concept: deep immunological targeting may enable KTx without apheresis in highly sensitized patients

Leon J, Aubert O, Devriese M, Anglicheau D, Zuber J et al. Kidney Int 2026



Leon J, Aubert O, Devriese M, Anglicheau D, Zuber J et al. Kidney Int 2026

Take-Home Messages

1. **Apheresis remains efficient for rapid antibody removal**
   Proof of clinical efficacy is missing for some conditions
   Benefit over Imlifidase ?

2. **New therapies target the source**
   Anti-CD38, bispecifics efficiently deplete plasma cells?

3. **The future may be improved sequential combination therapy** ***to*** *sustained plasma cell suppression*

4. **Evidence for new agents in transplant is still nascent** ***M****ostly case series so far*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Thank you

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