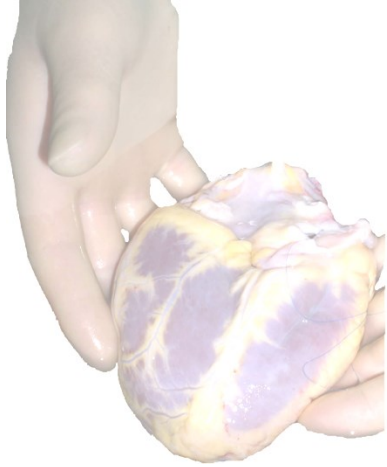
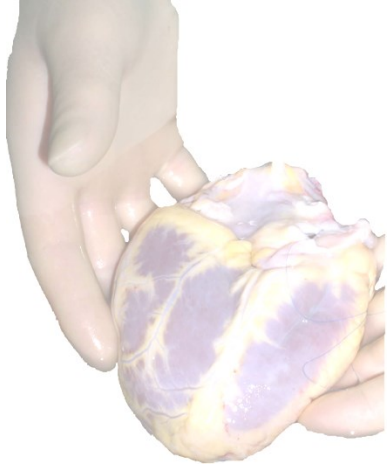


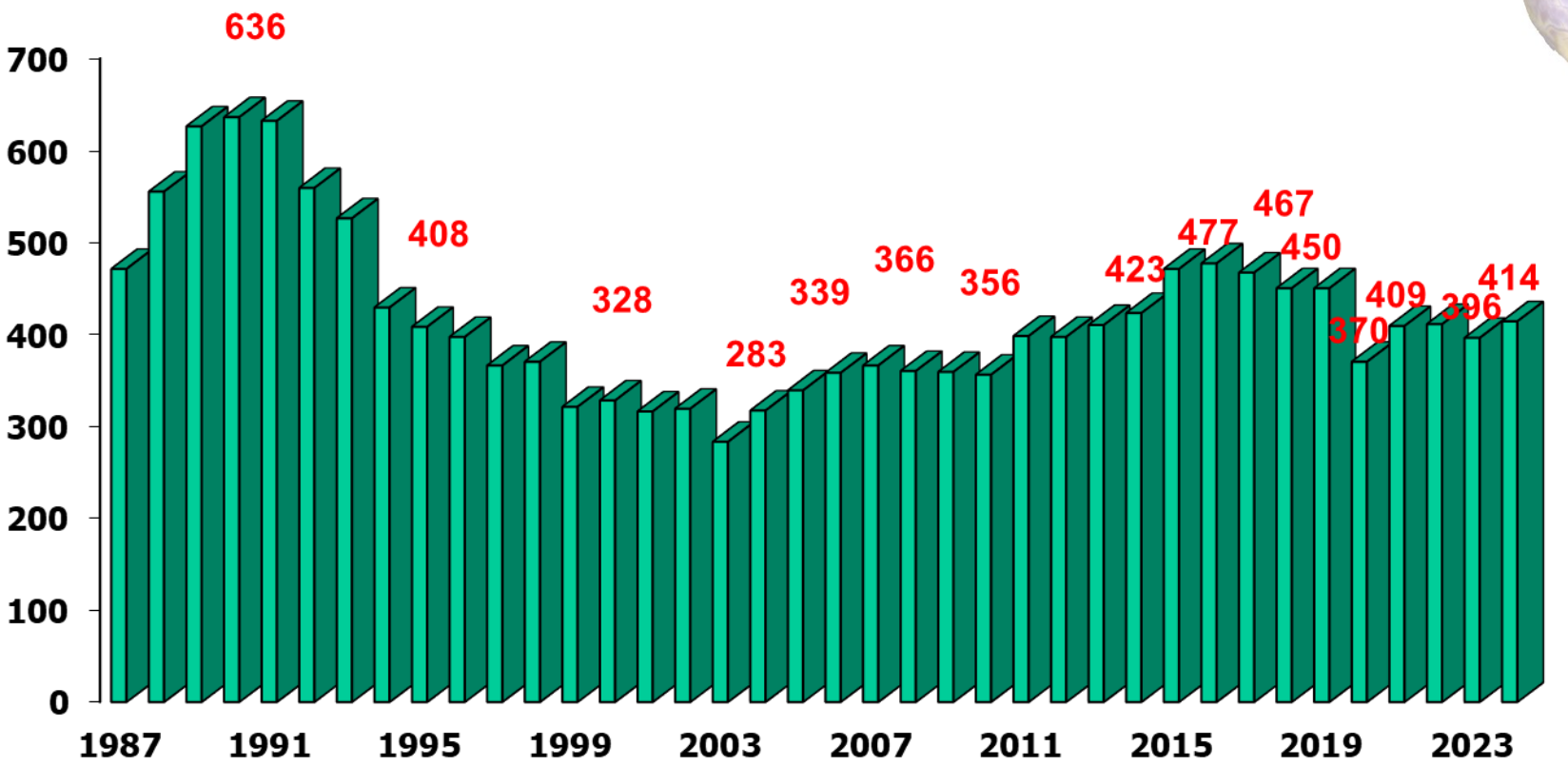
Rejet de greffe cardiaque et PCE

Congrès de la Société Française d'Hémaphérèse
Lyon le 29 janvier 2026

Dr Eric Epailly
Praticien Hospitalier
Transplantation cardiaque
Eric.epailly@chru-strasbourg.fr

Greffe cardiaque en France

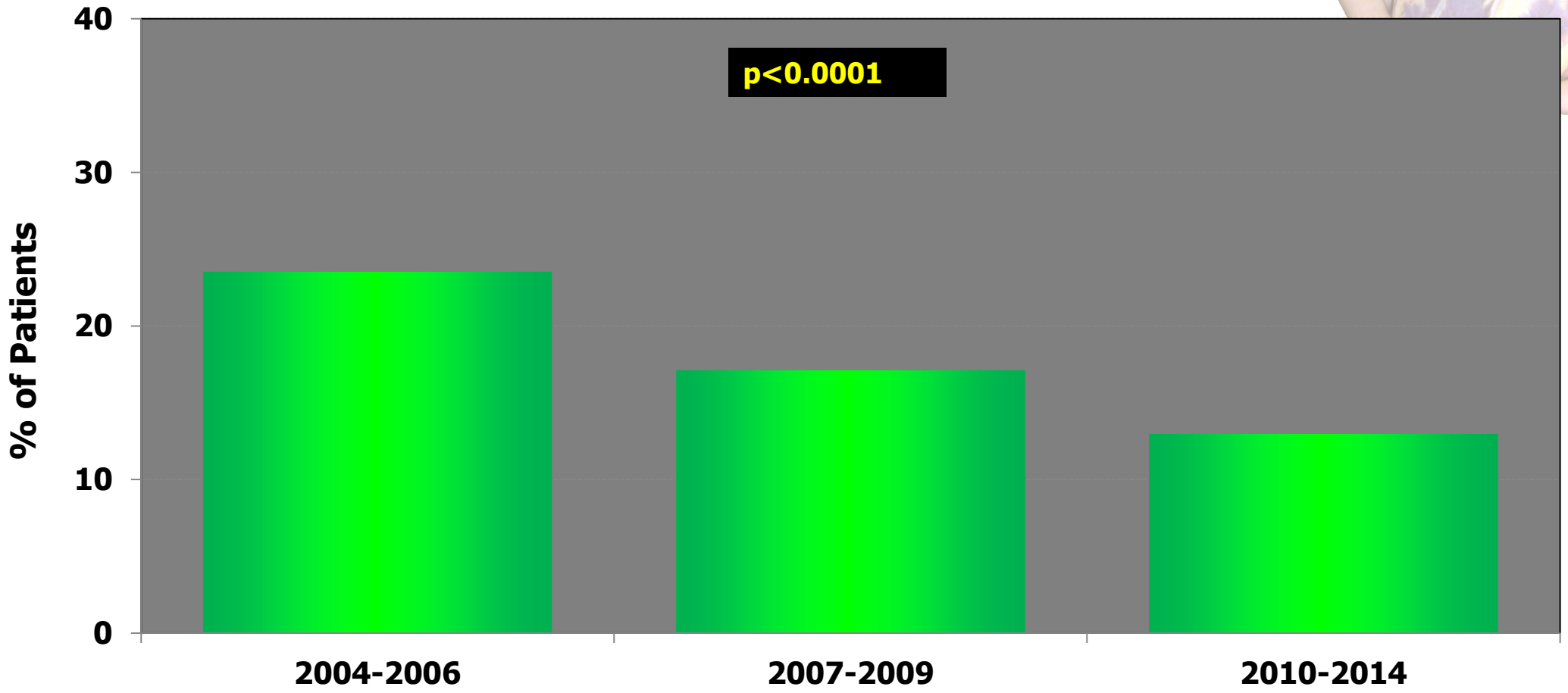




Rapport d'activité Agence de la BioMédecine 2024

Adult Heart Transplants

% of Recipients Experiencing *Treated* Rejection Between Transplant Discharge and 1-Year Follow-Up by Era



Analysis is limited to patients who were alive at the time of the follow-up.

Treated rejection = Recipient was reported to (1) have at least one acute rejection episode that was treated with an anti-rejection agent; or (2) have been hospitalized for rejection.

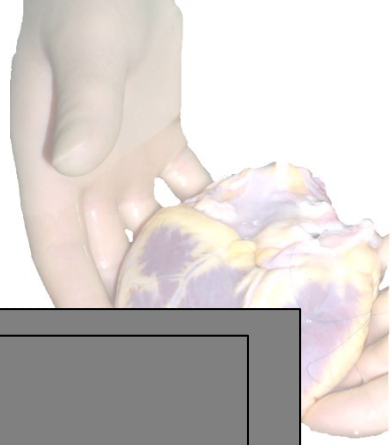
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

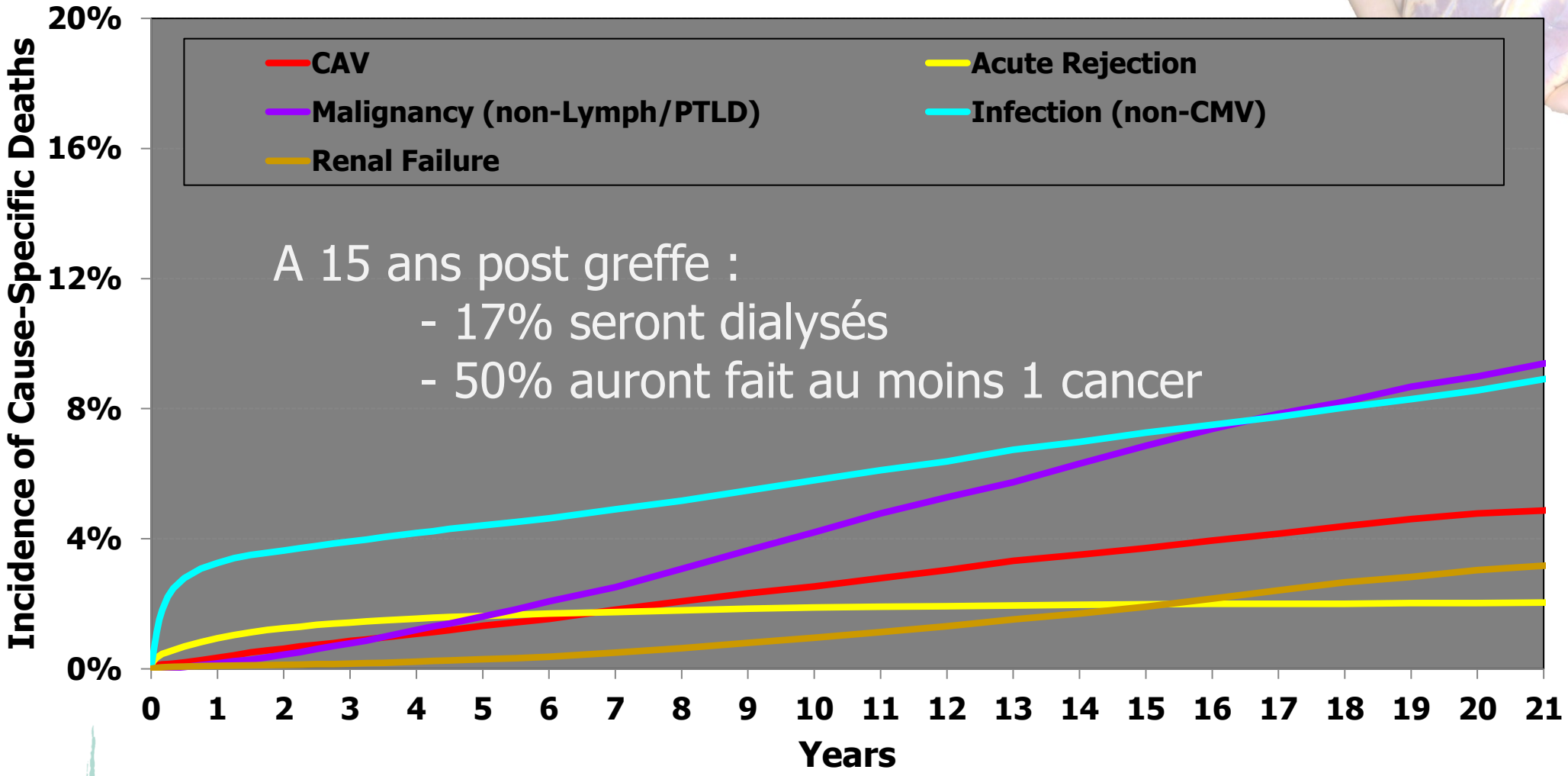
2017

2017 Oct; 36(10): 1037-1079

LES HOPITAUX UNIVERSITAIRES DE STRASBOURG

Transplanté cardiaques adultes
Causes de décès
(Transplants: January 1994 – June 2015)





2017

ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

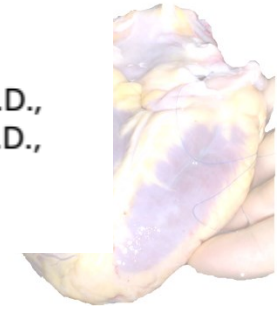
2017 Oct; 36(10): 1037-1079

LES HÔPITAUX UNIVERSITAIRES DE STRASBOURG

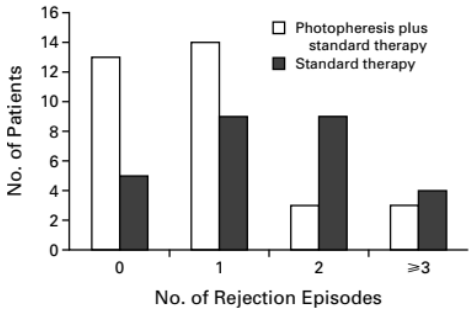
PHOTOPHERESIS FOR THE PREVENTION OF REJECTION IN CARDIAC TRANSPLANTATION

MARK L. BARR, M.D., BRUNO M. MEISER, M.D., HOWARD J. EISEN, M.D., RANDALL F. ROBERTS, M.D., UGOLINO LIVI, M.D., ROBERTO DALL'AMICO, M.D., PH.D., RICHARD DORENT, M.D., JOSEPH G. ROGERS, M.D., BRANISLAV RADOVANČEVIĆ, M.D., DAVID O. TAYLOR, M.D., VALLUVAN JEEVANANDAM, M.D., AND CHARLES C. MARBOE, M.D., FOR THE PHOTOPHERESIS TRANSPLANTATION STUDY GROUP

NEJM 1998



- Etude prospective randomisée multicentrique
- 60 patients consécutifs transplantés cardiaques suivi 6 mois
  - Bras Standard : Cya-aza-st
  - Bras ECP : Cya-aza-st + **ECP 24 sessions**
- Nombre de rejet aigus cellulaires dans le bras ECP p=0,04
  - Bras Standard : 1,44 épisodes par patients
  - Bras ECP : 0,91 épisodes par patients
- Complications rapportés à la photophérèse
  - Infection de catheter Serratia traité avec succès : 1 patient
  - Difficultés d'accès veineux : 6 patients



Clin Transplantation 2000: 14: 162–166
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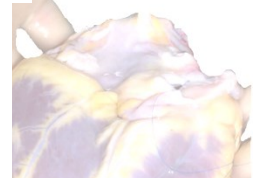
Clinical Transplantation
ISSN 0902-0063

Prophylactic photopheresis and chronic rejection: effects on graft intimal hyperplasia in cardiac transplantation



Mark L Barr, Craig J Baker, Felicia A Schenkel, Susan N McLaughlin, Bruce C Stouch, Vaughn A Starnes and Eric A Rose

Divisions of Cardiothoracic Surgery, University of Southern California, Los Angeles, CA and Columbia University, New York, NY

- Etude monocentrique randomisée
- 23 patients transplantés cardiaques suivi 2 ans
  - Bras Standard : Cya-aza-st N=13
  - Bras ECP : Cya-aza-st + **ECP 24 sessions** N=10
- Diminution des anticorps HLA (PRA) dans le groupe ECP à 3 mois ($p<0,03$) et 6 mois ($p<0,05$)

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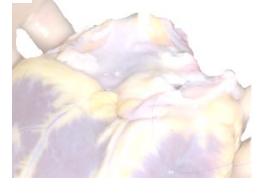
Clinical Transplantation
ISSN 0902-0063

Prophylactic photopheresis and chronic rejection: effects on graft intimal hyperplasia in cardiac transplantation



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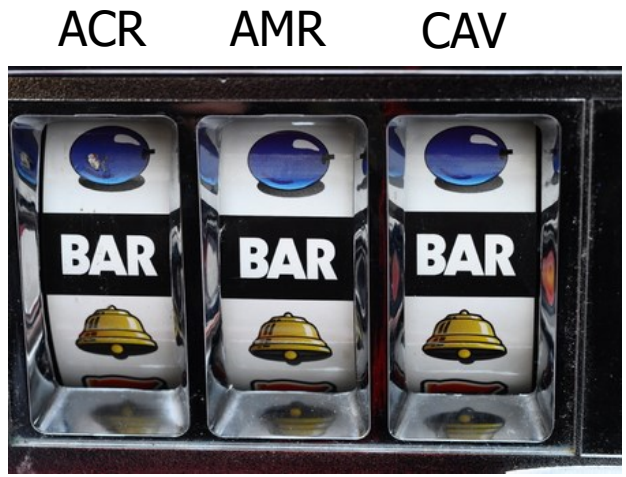
- Etude monocentrique randomisée
- 23 patients transplantés cardiaques suivi 2 ans
  - Bras Standard : Cya-aza-st N=13
  - Bras ECP : Cya-aza-st + **ECP 24 sessions** N=10
- IVUS : Epaisseur intimale significativement moins importante dans le bras ECP
  - 0,23mm ± 0,09 vs 0,49 mm ± 0,2 p<0,04 à 1 an
  - 0,28mm ± 0,08 vs 0,46mm ± 0,07 p<0,02 à 2 ans

Influence de la photophérèse sur le rejet en transplantation cardiaque

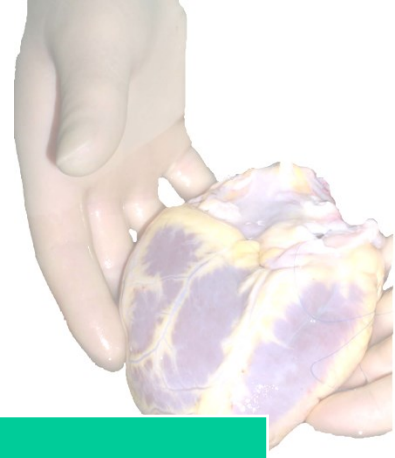
- ACR
  - Barr NEJM 1998
- CAV
  - Barr Clin Transpl 2000
- AMR
  - Barr Clin Transplant 2000

Influence de la photophérèse sur le rejet en transplantation cardiaque

- ACR
  - Barr NEJM 1998
- CAV
  - Barr Clin Transpl 2000
- AMR
  - Barr Clin Transplant 2000



Rejet aigu cellulaire
Littérature

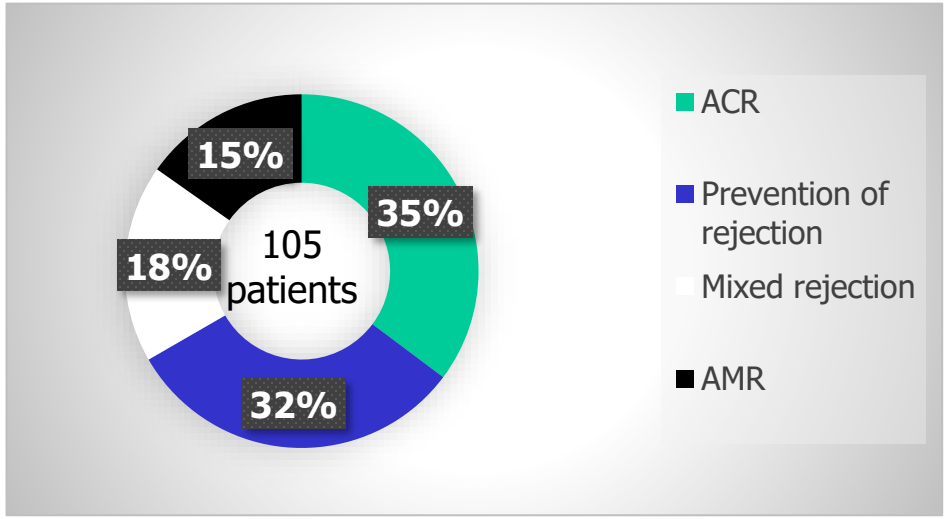


Author	Year	Nb Patients	
Rose	1992	4	High PRA Duration 12-14m : ↘ rejection ↘ PRA
Costanzo Nordin	1992	9	Steroids vs ECP : Same ACR incidence
Dall'Amico	1995	8	Adjuvant to standard IS : ↘ of 8 ↘ of rejection rate
Giunti	1999	6	Recurrent ACR Duration 6 m : ↘ of rejection rate
Dall'Amico	2000	11	Recurrent ACR Duration 6 m : ↘ of rejection rate
Lehrer	2001	4	4 ACR treated
Maccherini	2001	12	↘ ACR rate
Kirklin	2006	36	↘ ACR rate
Gokler	2021	28	IS Minimization

European multicenter study on the real-world use and clinical impact of extracorporeal photopheresis after heart transplantation

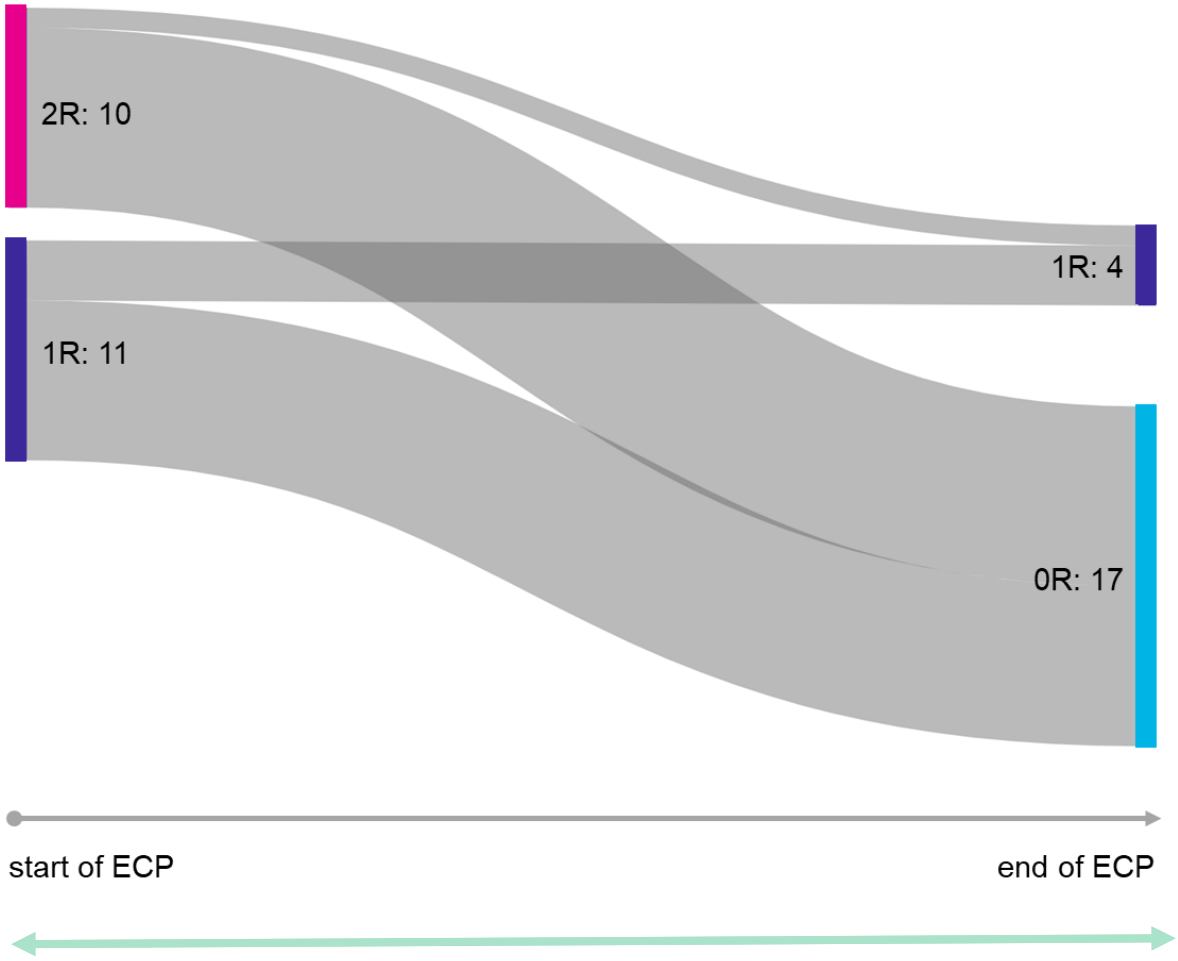
Markus J. Barten, MD,[a] Balázs Sax, MD,[b] Simon Schopka, MD,[c] Cristiano Amarelli, MD,[d] Eric Epailly, MD,[e] Benedetta Natali, MD,[f] Tímea Teszák, MD,[b] Johannes Gökler, MD,[g] Kathrin Borchert, MPH,[h] Julia Theil, MPH,[h] Andy Ingram, MBA,[i] and Andreas Zuckermann, MD[g]

- 7 centres européens
- Etude retrospective
- Patients transplantés cardiaques ayant commencé un traitement par photophérèse entre 2015 et 2021
- Données extraites des dossiers



Barten JHLT 2023
Hambourg, Regensburg, Strasbourg, Budapest, Siena, Naples, Vienna

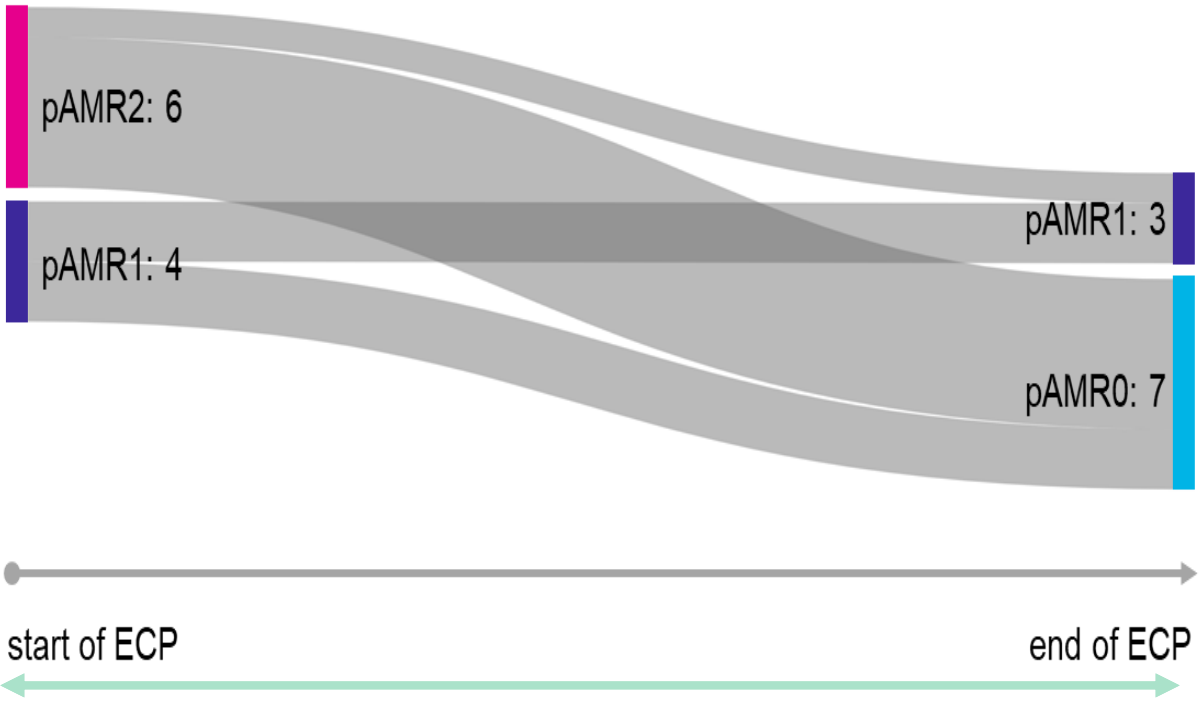
Résultats : Rejets aigus cellulaires
21 patients avec photophérèse terminée



Durée moyenne de photophérèse = 6.8 mois

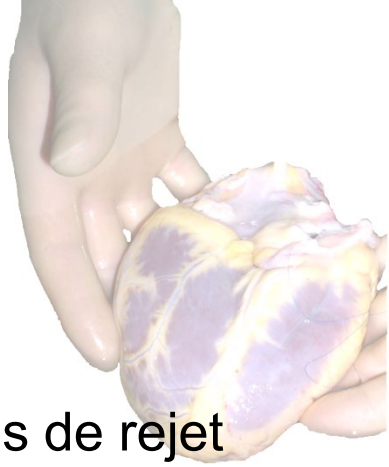
Résultats : Rejets aigus humoraux

10 patients avec photophérèse terminée

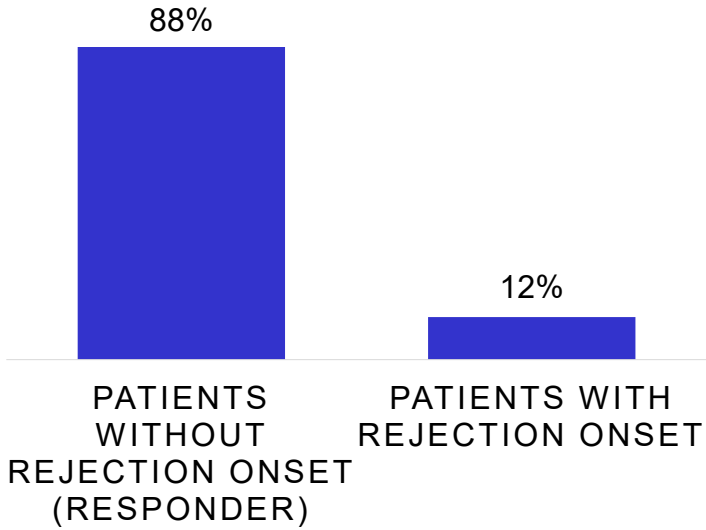


Durée moyenne de traitement par photophérèse = 6.1 mois

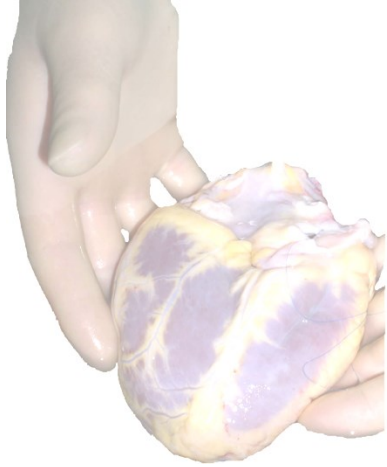
Résultats
Groupe prévention



- 33 patients considérés à haut risque de rejet, 29 (88%) indemnes de rejet après le début de la photophérèse sur un suivi de 2 ans.



- 4 patients avec rejet aigu cellulaire. 2 patients ont dévelopé des DSA sans rejet.

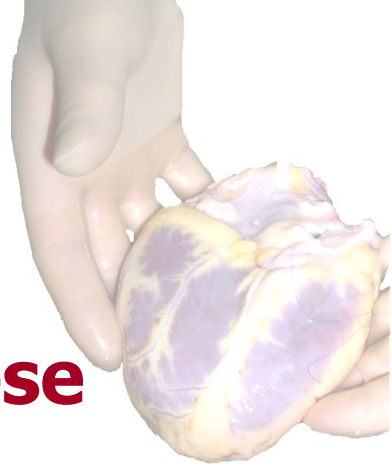


Resultats
Survival N=105

- Survie 95%
- Suivi moyen de 2 ans

- 5 patients décédés (3 après la fin du traitement)
  - Insuffisance cardiaque : 2
  - Mort subite: 1
  - Non définie : 1
  - Rupture d'anévrysme aortique : 1

Aucun décès lié à la photophérèse

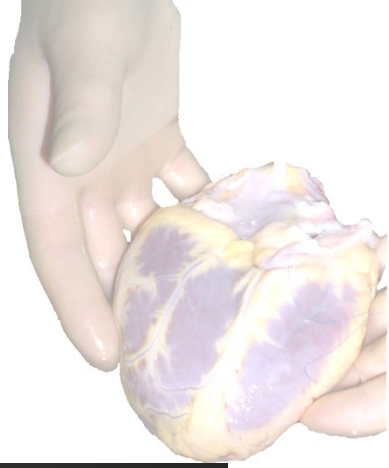


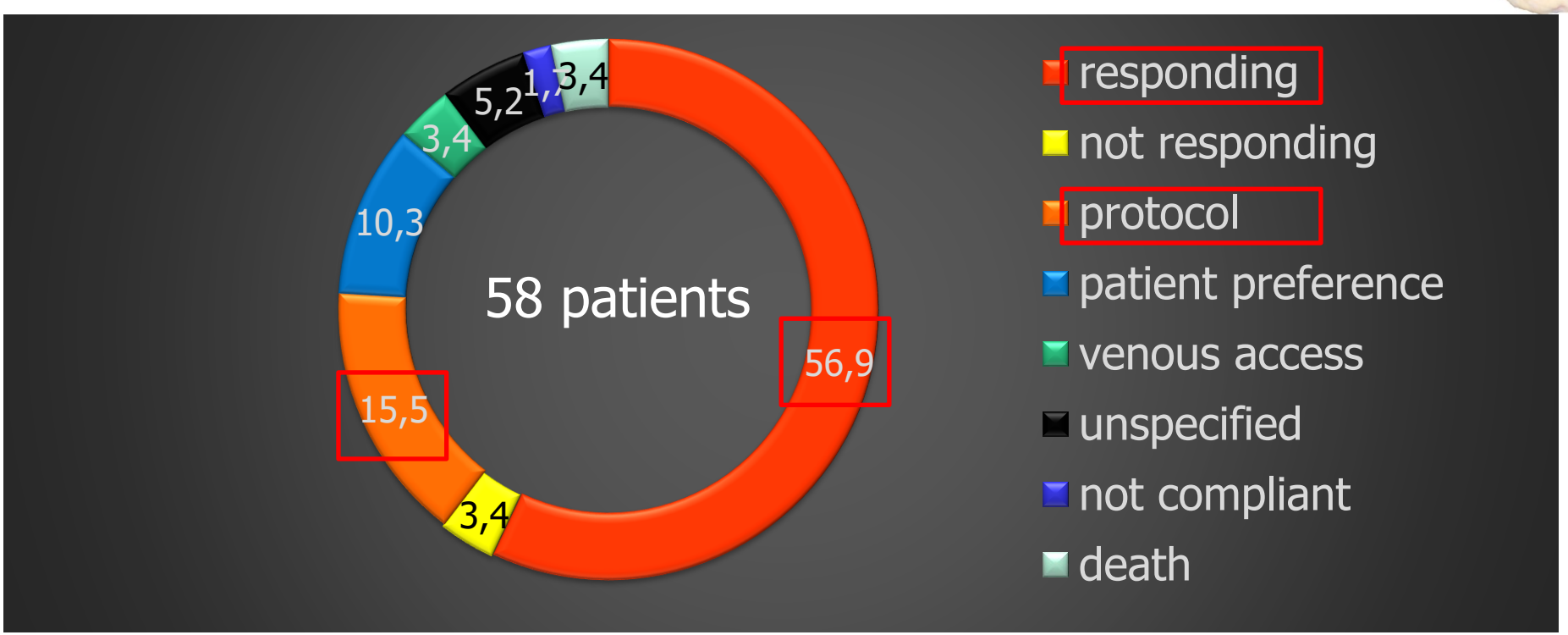
Resultats

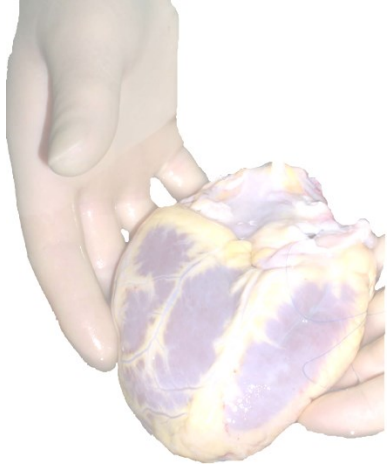
Effets indésirables liés à la photophérèse

- 78 événements chez 18 patients (17%)
  - Accès veineux insuffisants : 13 patients (2 arrêt de traitement)
  - Anémie : 6 patients (6%)
  - Hypotension 3 patients (3%)
  - Fièvre : 1 patients (1%)
  - indéterminés : 2 patients (2%)

Raison de l'arrêt

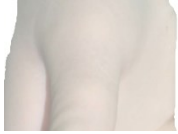




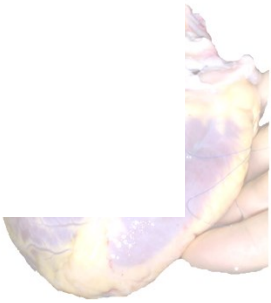


Limitations de l'étude

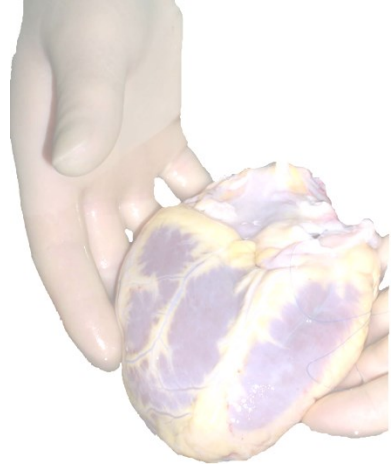
- Etude non comparative
- Population inhomogène (vraie vie)
- Protocoles inhomogènes (vraie vie)
- Données non auditées
- Faibles effectifs



The International Society for Heart and Lung Transplantation (ISHLT) Guidelines for the Care of Heart Transplant Recipients



Costanzo 2010	Velleca 2023
Additional approaches that can be considered for recurrent or resistant acute cellular rejection include methotrexate pulse therapy, photopheresis and total lymphoid irradiation. Class IIb, Level of Evidence: B	Recurrent or resistant acute cellular rejection that occurs after treatment with CS and cytolytic immunosuppressive therapy and optimization of the patient's maintenance immunosuppressive regimen can be treated with photopheresis or total lymphoid irradiation **Class IIa, Level of Evidence: B**



AHA Scientific Statement

Antibody-Mediated Rejection in Cardiac Transplantation: Emerging Knowledge in Diagnosis and Management

A Scientific Statement From the American Heart Association

Endorsed by the International Society for Heart and Lung Transplantation

Monica M. Colvin, MD, MS, Chair; Jennifer L. Cook, MD, Co-Chair; Patricia Chang, MD;

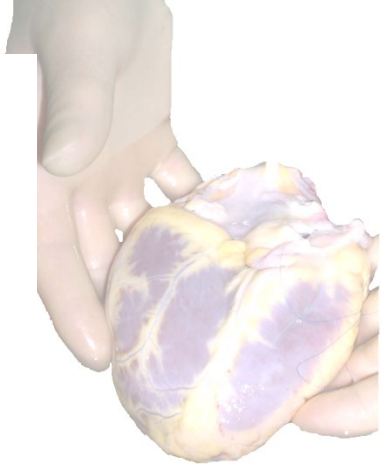
Table 8. Summary of Commonly Used Agents for AMR

Therapeutic Modality	Mechanism of Action	Adverse Events	Dose	Frequency	Duration	Cost
Corticosteroids	Upregulation of anti-inflammatory gene expression, mediated by activated protein-1 and NF-κB	Dyslipidemia, hyperglycemia, osteoporosis, leukocytosis	Oral: 1–3 mg/kg IV: 250–1000 mg	Daily	3 d	$
IVIg	Blockade of Fc-q receptor Complement inhibition Downregulates B-cell receptor Neutralizes circulating antibody and cytokines	Headache Chills Rigors Fever Myalgia Volume overload	1–2 g/kg in 2–4 divided doses	1–3 Times weekly	Variable	$$$$
Tissue plasma exchange (plasmapheresis)	Nonselective removal of circulating alloantibody, proteins, cytokines; IAP removes only immunoglobulins	Rebound antibodies Bleeding diathesis Hypotension Allergic reaction Transmission of blood-borne pathogens	1–7 Sessions/wk, 1–4 weekly cycles Exchange 1–2 times the blood volume with FFP or albumin as replacement	1–7 Sessions	Variable	$$$
Photopheresis	Upregulation of costimulatory molecules, downregulation of T cells, immunoregulation via T-regulatory cells	Vascular access complications, skin erythema, pruritus, nausea, rare drug-induced lupus or scleroderma-like syndrome	Oral: 0.6 mg/kg (target level ≥50 ng/mL 2 h after ingestion) or 25 mg/m²	Variable	Up to 6 mo	$$$$

Coût d'une procédure en France: 1387 euros

Colvin Circulation 2015

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue



Anand Padmanabhan[1] | Laura Connelly-Smith[2] | Nicole Aqui[3] | Rasheed A. Balogun[4] | Reinhard Klingel[5] | Erin Meyer[6] | Huy P. Pham[7] | Jennifer Schneiderman[8] | Volker Witt[9] | Yanyun Wu[10] | Nicole D. Zantek[11] | Nancy M. Dunbar[12] |

Disease	TA modality	Indication	Category	Grade	Page
Transplantation, cardiac	ECP	Cellular/recurrent rejection	II	1B	331
	ECP	Rejection prophylaxis	II	2A	
	TPE	Desensitization	II	1C	
	TPE	Antibody mediated rejection	III	2C	

J Clin apher 2019

Current Usage of Extracorporeal Photopheresis in Solid Organ Transplantations in Europe: A Narrative Review

Sarah-Jane Cashmore[1], Markus Johannes Barten[2], Fritz Diekmann[3], Eric Epailly[4], Andrew J. Fisher[5], Andrew R. Gennery[5], Ben Gibbons[1], Johannes Gökler[6], Julie Guest[7], Anne-Elisabeth Heng[8], James A. Hutchinson[9], Teresa Rampino[10], Robin Vos[11] and Luciano Potena[12]*

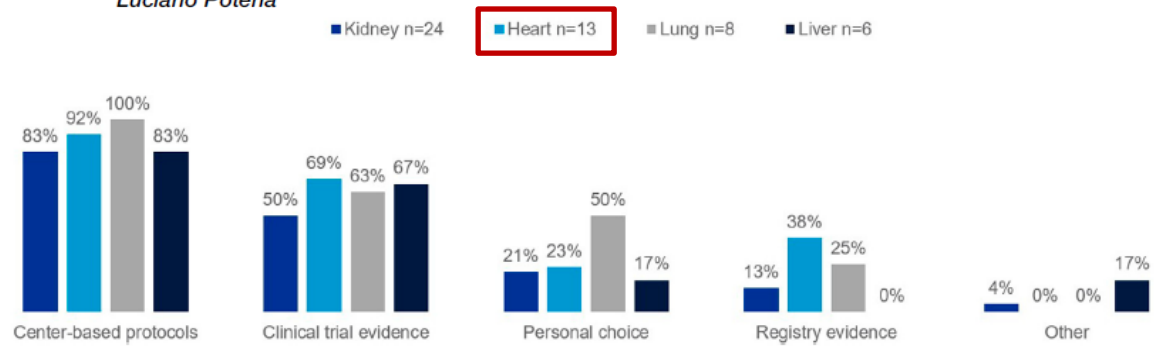
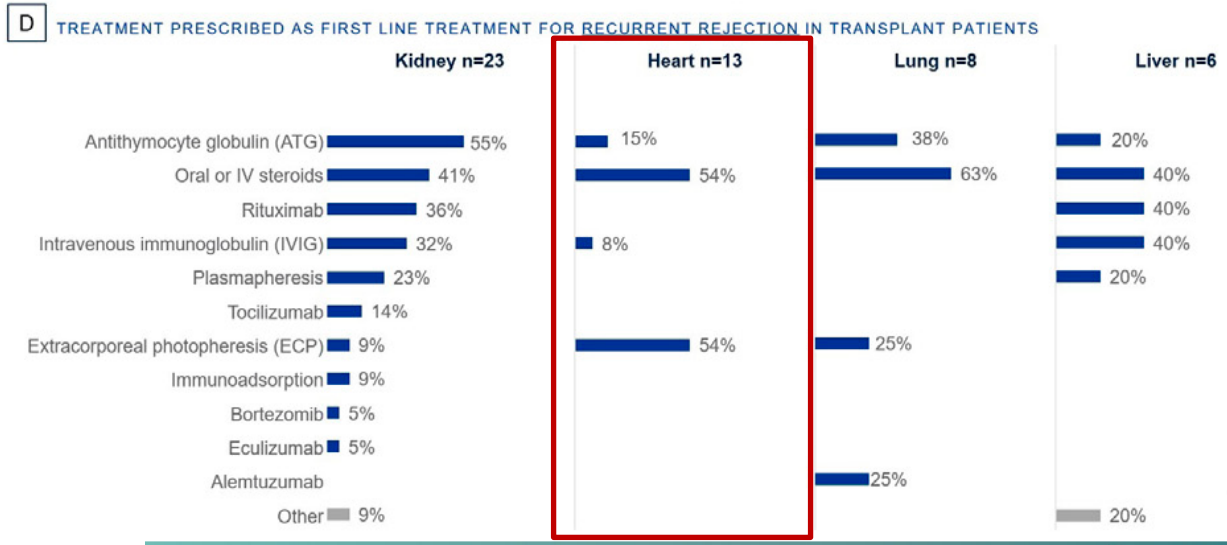


FIGURE 1 | Percentage of European clinicians using each of the following as part of their clinical rationale for approach taken regarding treatments to prevent against rejection in transplant recipients, by organ type.



Cashmore Transpl int 2025

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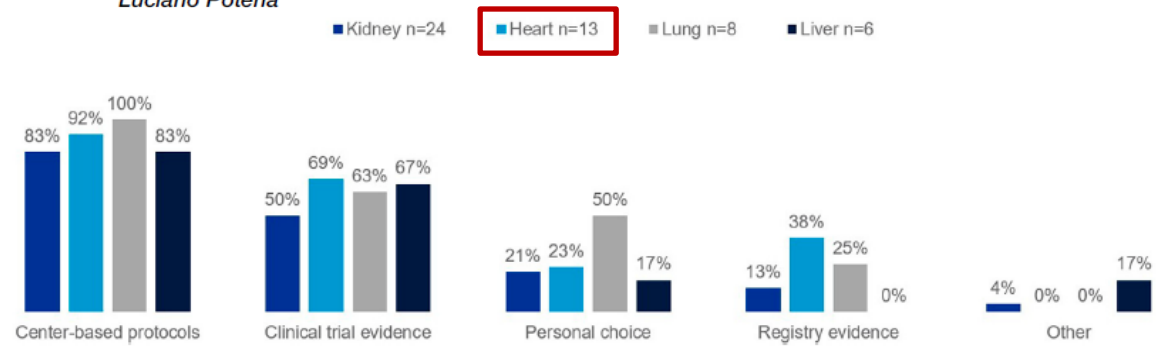

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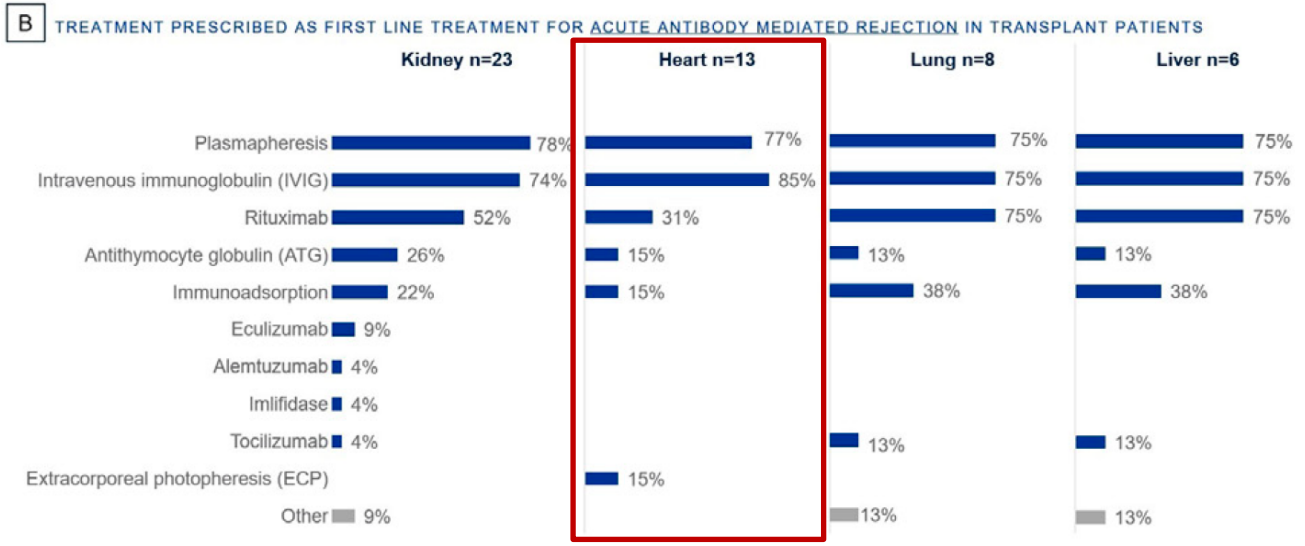


Cashmore Transpl int 2025

Accessibilité à la photophérèse ?

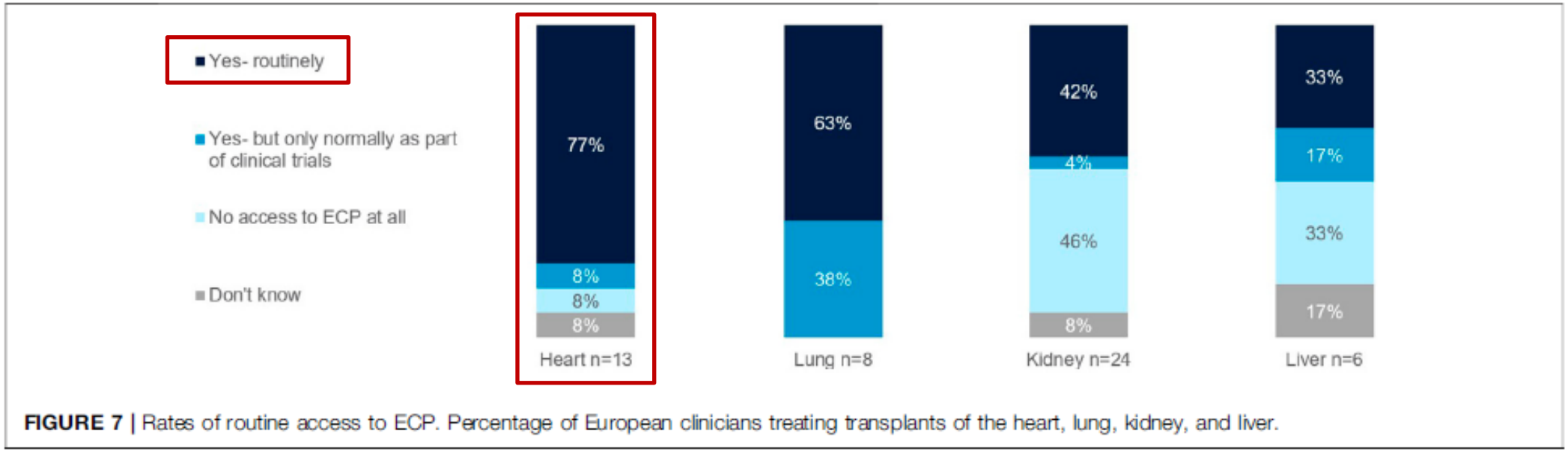


FIGURE 7 | Rates of routine access to ECP. Percentage of European clinicians treating transplants of the heart, lung, kidney, and liver.

Cashmore Transpl int 2025

Photophérèse et baisse des CNI

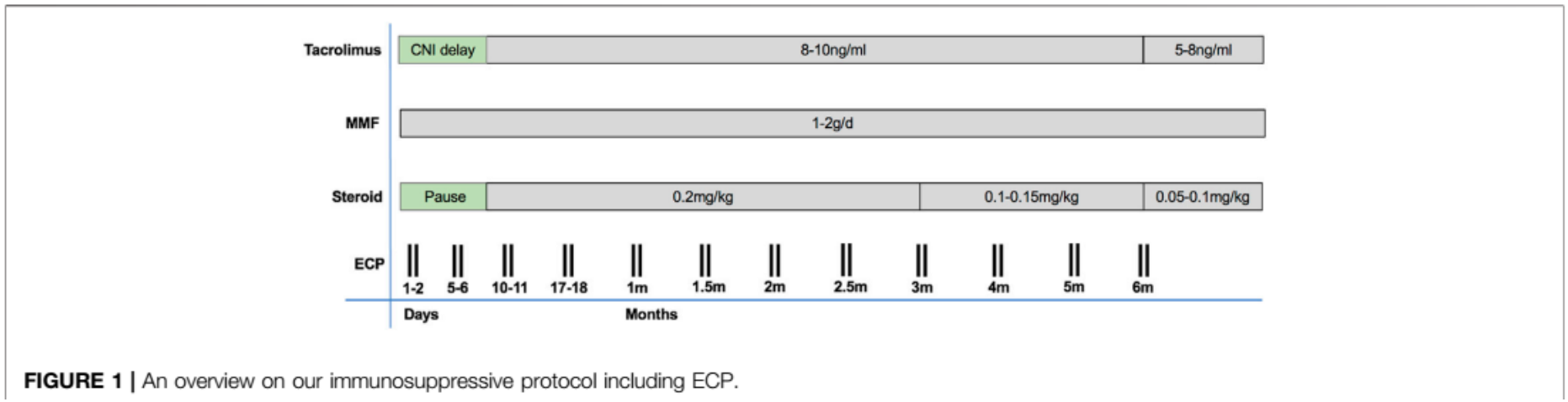
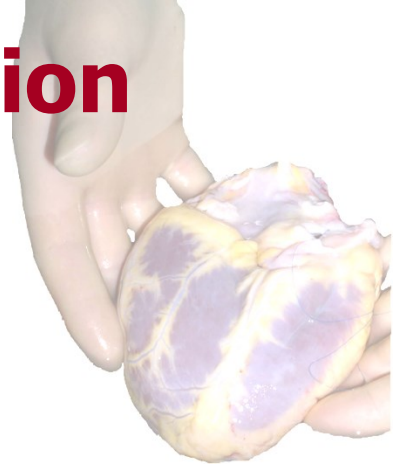


FIGURE 1 | An overview on our immunosuppressive protocol including ECP.

- 28 patients transplantés cardiaques
- Pas d'induction, CNI introduction à J3
- Tacro résiduel cible : 8-10ng/ml and 5-8ng/ml après M6
- ACR $\geq$ 2R à 1 an : 14,3% (N=4)

Gokler Transpl int 2022

Minimisation de l'immunosuppression épargne rénale



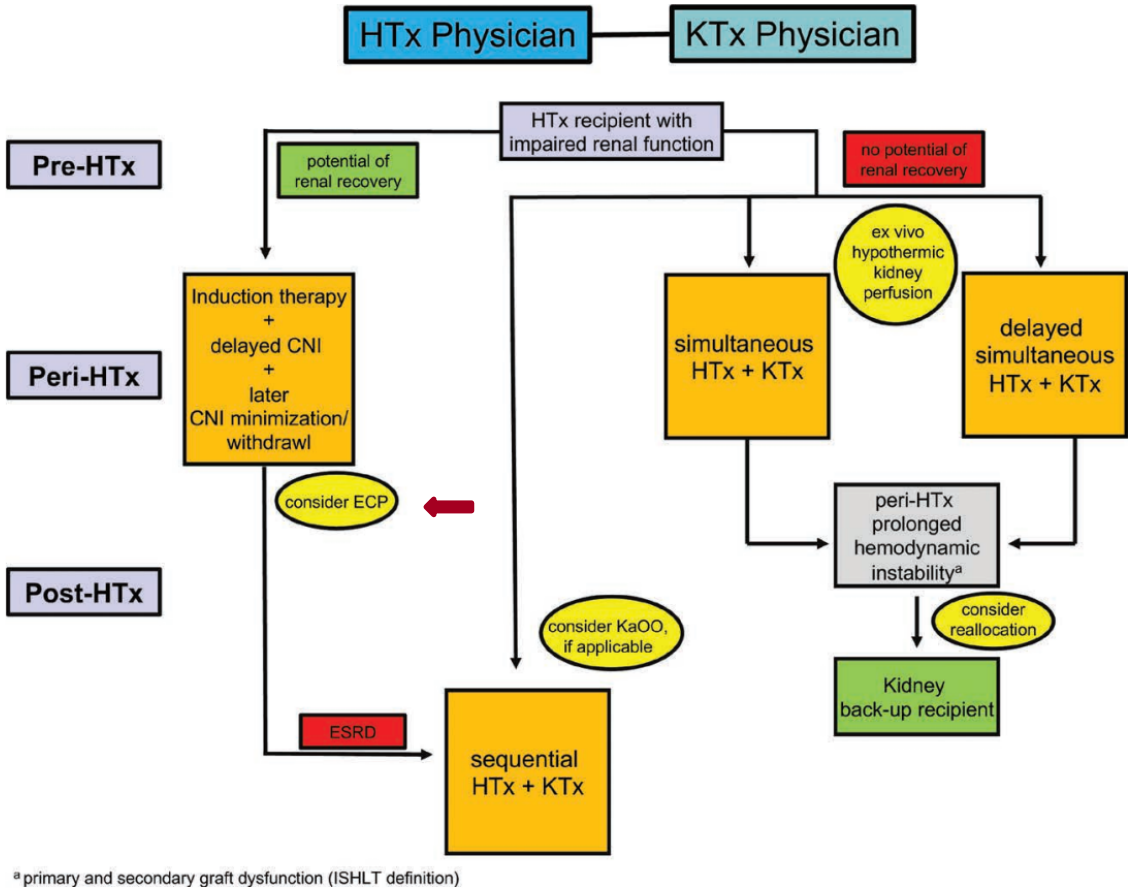
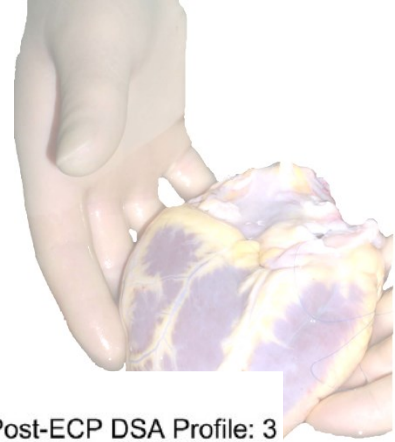


FIGURE 1. Proposal for an algorithm for HTx recipients with impaired renal function based on an interdisciplinary work-up between HTx and KTx physicians to preserve kidney function after HTx alone, after sHKTx, or sequential HTx and KTx. For sHKTx, the proposed use of ex vivo hypothermic kidney perfusion by Lutz et al in this issue seems to be favorable. CNI, calcineurin inhibitor; ECP, extracorporal photophoresis; ESRD, end-stage renal disease; HTx, heart transplantation; ISHLT, International Society of Heart and Lung Transplantation; KaOO, Kidney after Other Organs; KTx, kidney transplantation; sHKTx, simultaneous HTx and KTx.

Barten Transplantation 2023

Extracorporeal Photopheresis in the Treatment of Cardiac Allograft Rejection in the Modern Era: A Single-Center Experience

Gal Rubinstein[1] | Andrea Fernandez Valledor[1,2] | Cathrine M. Moeller[1] | Julia Baranowska[1] | Daniel Oren[1] | David Kyung Taek Oh[1] | David Bae[1] | Adil Yunis[1] | Dor Lotan[1] | Afsana Rahman[1] | Jayant K. Raikhelkar[1] | Justin A. Fried[1] | Ersilia M. DeFilippis[1] | Kevin J. Clerkin[1] | Farhana Latif[1] | Gabriel T. Sayer[1] | Nir Uriel[1]



Etude rétrospective
15 patients
suivi médian 11 mois
Immunosuppression très inhomogène

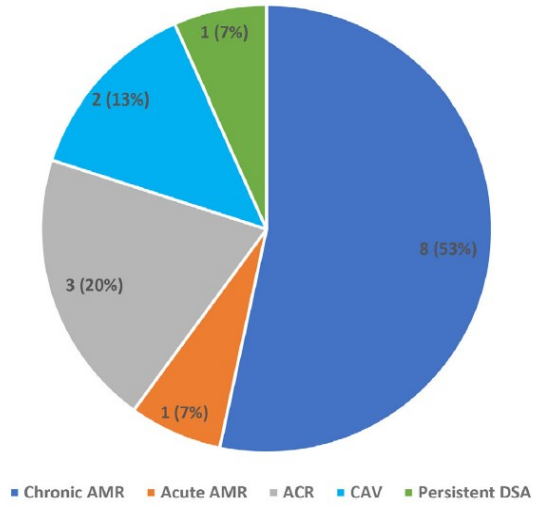


FIGURE 2 | Indications for ECP therapy.

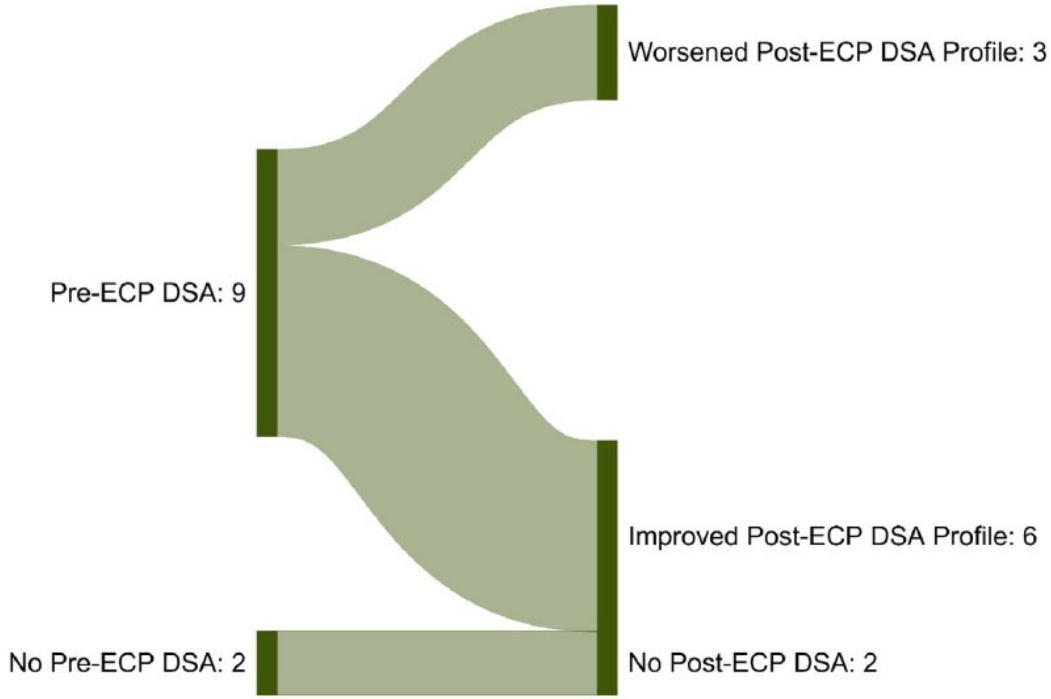


FIGURE 4 | DSA profile trend pre- and post-ECP.

Complications :

2 infections liées au KT, 1 thrombose de KT
2 décès défaillance multi-organes
1 Bkvirus, 2 cancers cutanés
1 retransplantation pour rejet humoral résistant

Les Hôpitaux Universitaires de STRASBOURG

Extracorporeal photopheresis in the treatment of cardiac allograft rejection: A single-centre experience

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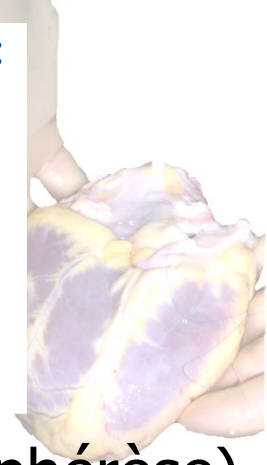
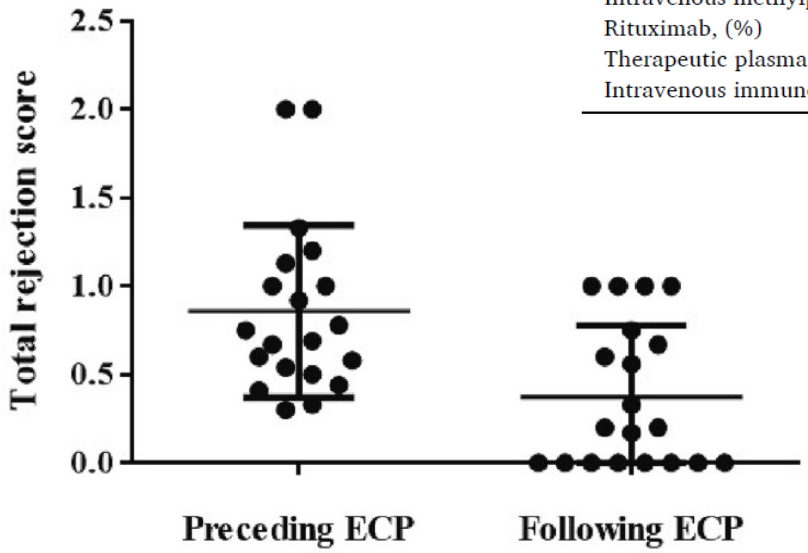


22 patients en rejet (cellulaire humoral ou mixte traités par photophérèse)

Additional immunosuppressive therapy in the ECP patient cohort.

	HTx patients (n = 22)
Intravenous methylprednisolone, (%)	14 (64%)
Rituximab, (%)	1 (4.5%)
Therapeutic plasma exchange, (%)	5 (23%)
Intravenous immunoglobulin, (%)	5 (23%)



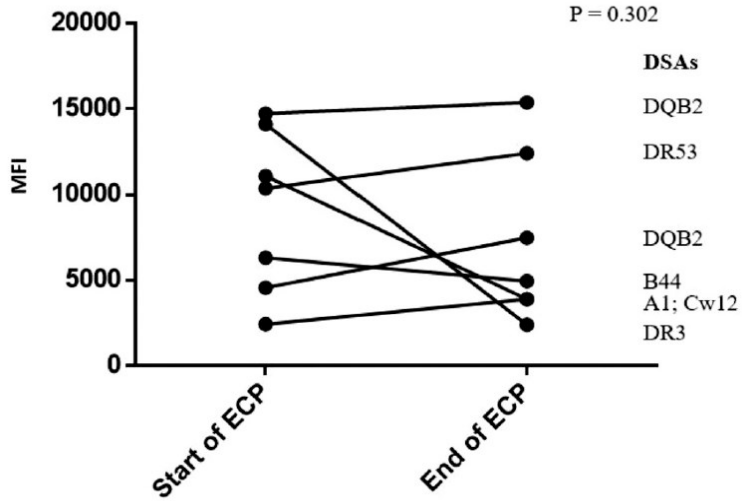
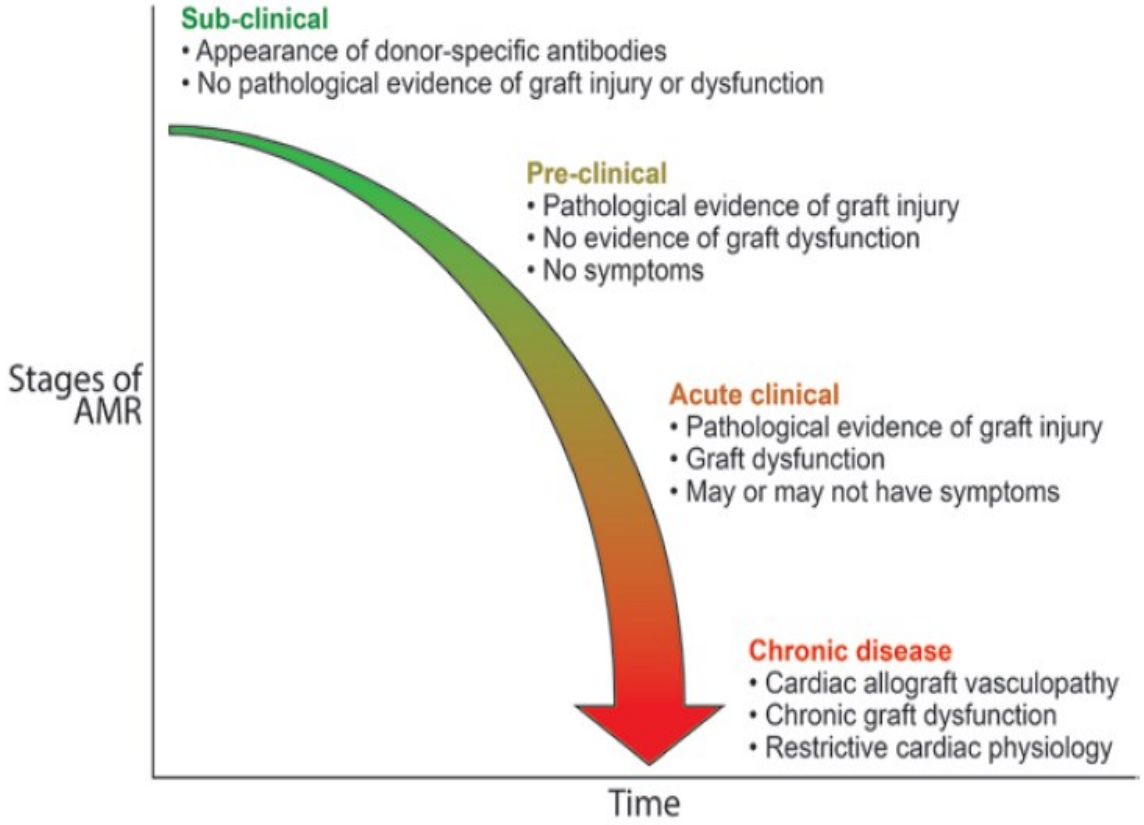


Fig. 1. Total rejection score at initial and last ECP treatments.
ECP = extracorporeal photopheresis.
*Statistical significance after Wilcoxon matched-pairs signed-rank test.

Transplant immunol 2023

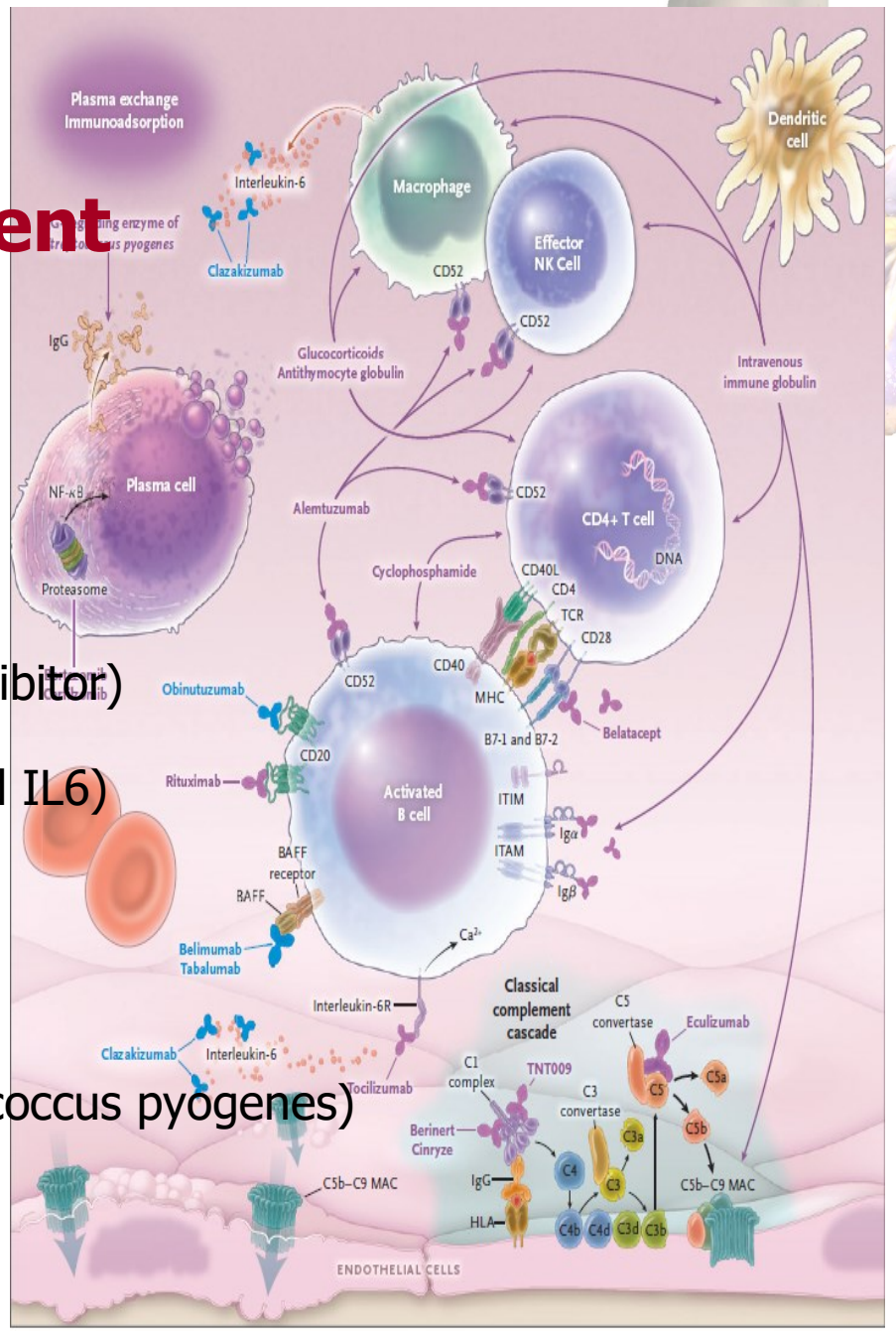
Continuum clinique du rejet humoral



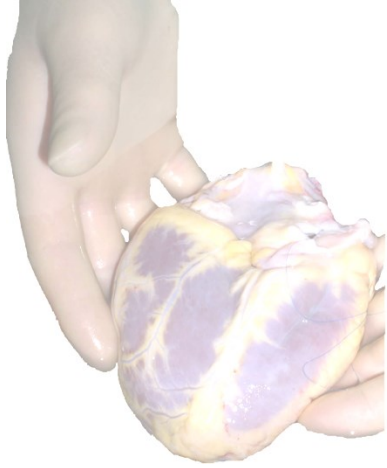
Colvin 2015

AMR :
No standardized treatment

- Plasma exchange
  - FDA approved
- IVIG
  - FDA approved
- Rituximab (antiCD20)
  - Rituxerah
- Bortesomib Carflizomib (proteosome inhibitor)
  - Bortejject
- Tocilizumab Clazakizumab (AntiIL6R and IL6)
  - Ongoing clinical trial
- Eculizumab (antiC5)
  - Ongoing clinical trial
- C1q esterase inhibitor
  - Ongoing clinical trial
- IdeS (IgG-degrading enzyme of streptococcus pyogenes)
  - Not evaluated



Loupy NEJM 2018



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Wiley Periodicals Inc.

doi: 10.1111/ajt.13721

Editorial

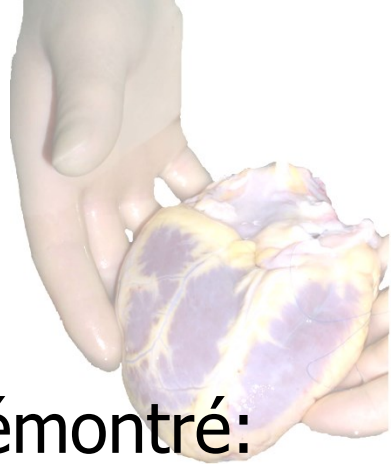
Therapeutics for Antibody-Mediated Rejection: A Slippery Slope Into Confusion

R. A. Montgomery*

« A field awash in the use of unproven, off-label medications »

- Rituximab : no level 1 evidence
- Eculizumab : (+ plasmapheresis) 1 single center single arm with historical controls
  - 4263 euros per 300mg (300 000 euros/years)
- C1-INH : 6 patients, change in DSA C1q status from 6/6 to 1/6 positive (p = 0.0253) compared to historical cohort 21 pts

Viglietti 2016



Conclusion

- La photophérèse après transplantation cardiaque a démontré:
  - Un effet bénéfique sur le rejet cellulaire humoral et « chronique » (Barr)
  - Un effet immunomodulateur permettant un passage à un état plus tolérant
  - Des effets secondaires mineurs
  - Un coût modéré
- La photophérèse est une option pour traiter le rejet humoral comme mentionné dans les recommandations récentes en transplantation cardiaque
- Des études (registre, essais cliniques) restent à faire