9. Ulusal
Transplantasyon İmmünolojisi ve Genetiği Kongresi

DESENSİTİZASYON MU ÇAPRAZ NAKİL Mİ?

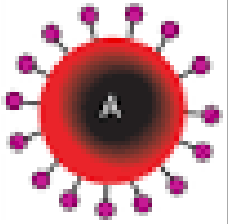
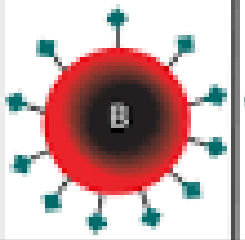
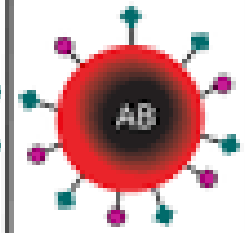
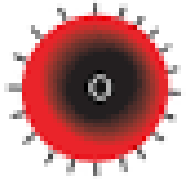
Dr. Ebru Sevinç Ok

Acıbadem Kent Hastanesi

Hasta kan grubu	Verici potansiyeli
0 kan grubu **%34**	%34
A kan grubu **%42**	%76
B kan grubu **%16**	%50
AB kan grubu **%8**	%100

Hastaların 1/3 ü kan grubu uyumsuzluğu
1/3 sensitizasyon nedeni ile nakil olamıyor.

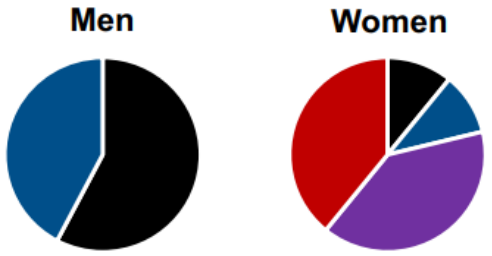
Sensitizasyon-Kan Grubu

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies present	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens present	 A antigen	 B antigen	 A and B antigens	No antigens

A kan grubunda %20 A2

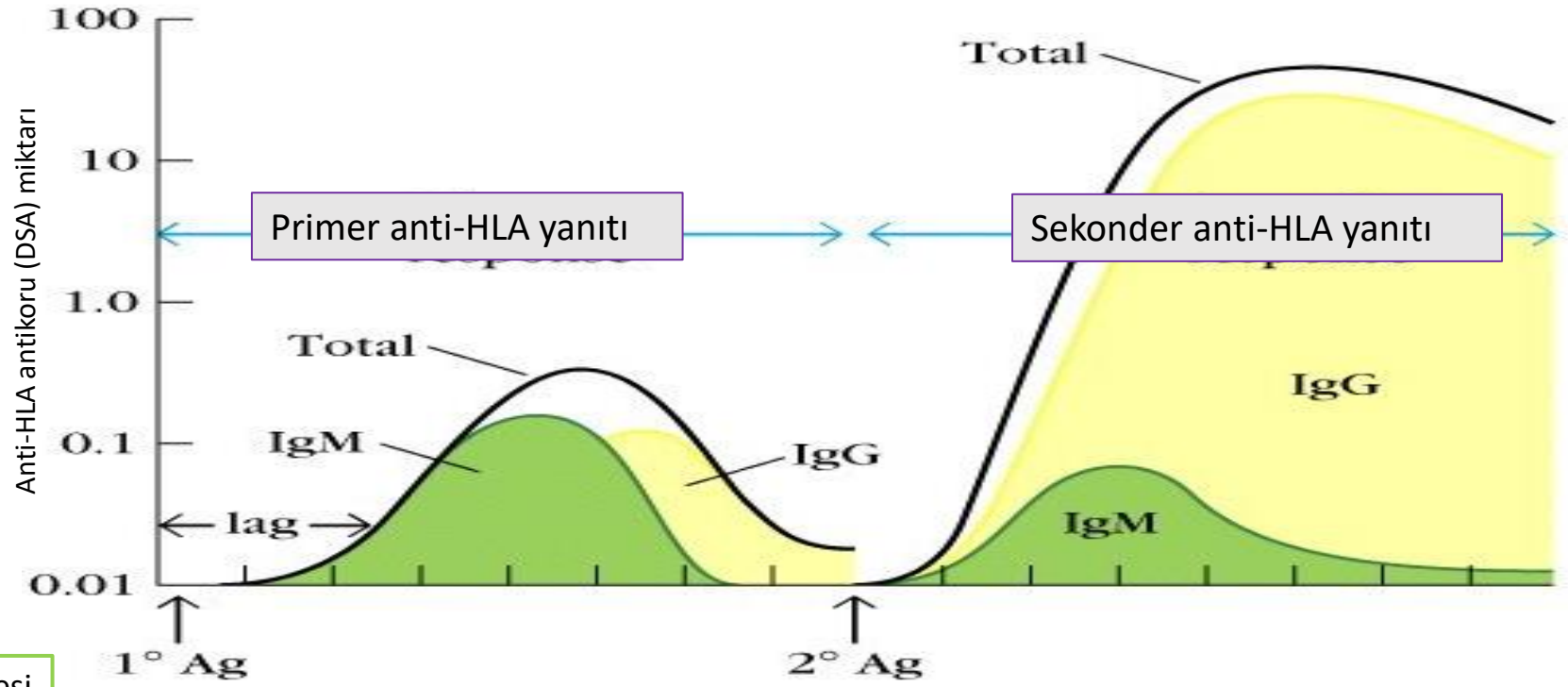
İmmunolojik özellik A1>B>**A2**

Sensitizasyon-Anti-HLA



- None
- Transfusion
- Pregnancy + Transfusion
- Pregnancy alone

TRANSPLANTASYON!



T Hücresi

B Hücresi

- Kısa ömürlü plazma hücresi
- Uzun ömürlü plazma hücresi
- Memory B hücresi

Serolojik hafıza — CD-FXM Elisa,Luminex

Hücresel hafıza — Elispot, florospot, Elisa

Transplantasyonda Risk Tanımlama

ENGAGE, 2021

HUMORAL RISK

RISK CATEGORIES & MANAGEMENT

1. Day-zero DSA with positive CDC
=> Tx impossible. Require desensitization before Tx

2. Day-zero DSA with positive flow and negative CDC
=> Tx possible but very high risk for acute AMR and accelerated chronic AMR. Require adaptation of follow up and maintenance IS

3. Day-zero DSA with negative flow
=> Tx possible with risk for acute AMR, and acceptable medium-term graft survival. Require adaptation of follow up and maintenance IS

4. Absence of day-zero DSA but potential cellular memory against donor HLA
=> Tx possible with risk for AMR increased.

4.a. Probable cellular memory if :
-historical DSA
-pregnancy and/or previous transplant with repeat Ag
4.b. Possible cellular memory if :
-transfusion(s) with no information on blood donors

5 no DSA and no cellular memory
=> Tx possible lower risk for AMR but de novo DSA still possible
NB: patient with day-zero non DSA HLA antibodies are "good humoral responders" with possible increased risk for subsequent de novo DSA generation

Figure 4 ENGAGE's proposal for categorization of the humoral risk of solid organ transplant candidates.

STAR, 2017

HUMORAL MEMORY

SEROLOGICAL MEMORY
CDC-XM (+)/(-)
Flow-XM (+)/(-)
DSA (+)
Aktif Memory
CD-FXM
Elisa,Luminex

CELLULAR MEMORY
CDC-XM (-)
Flow-XM (-)
Historical DSA (+)
Latent Memory
Elispot, florospot, Elisa

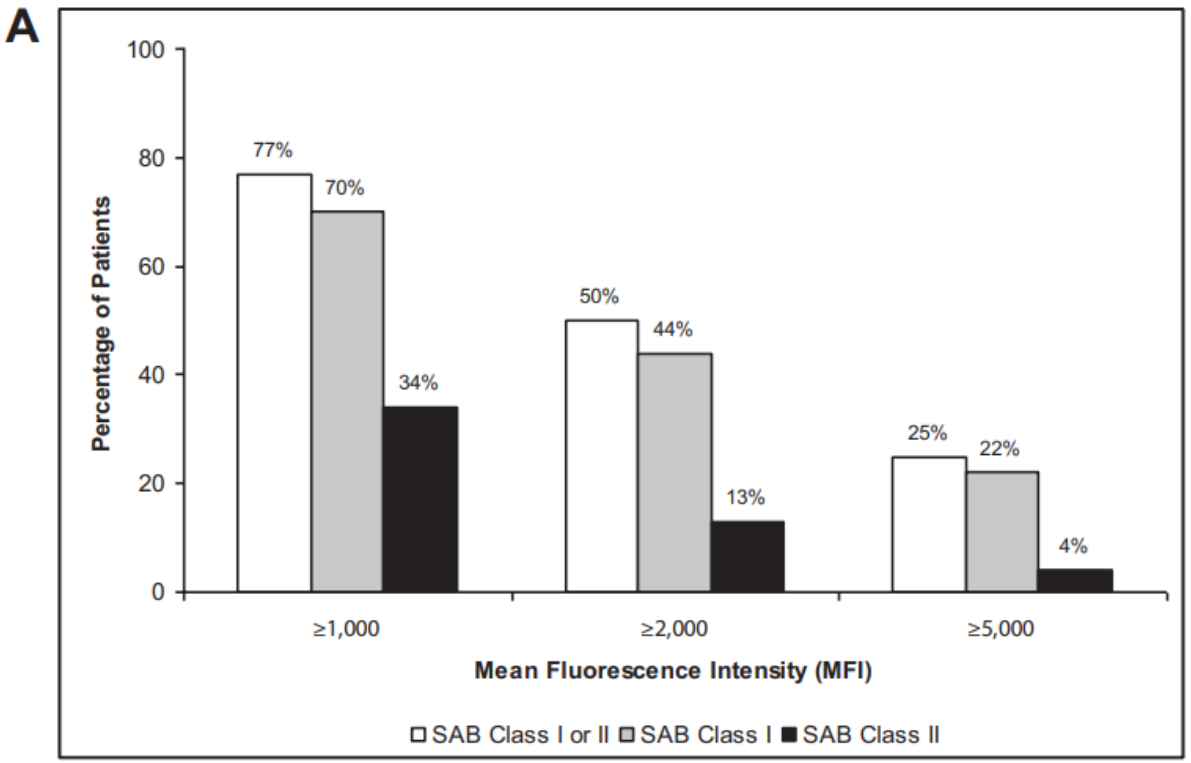
NAIVE
CDC-XM (-)
Flow-XM (-)
DSA (-)
Latent Memory

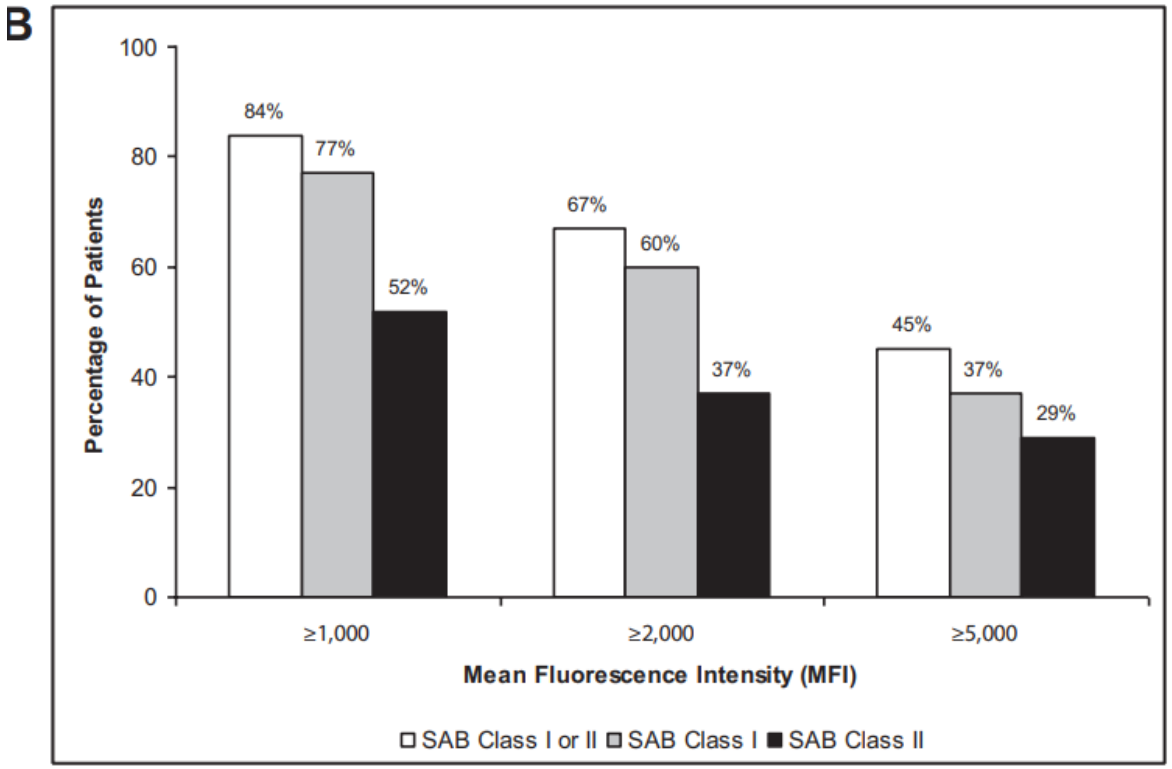
Influence of Test Technique on Sensitization Status of Patients on the Kidney Transplant Waiting List

American Journal of Transplantation 2013;

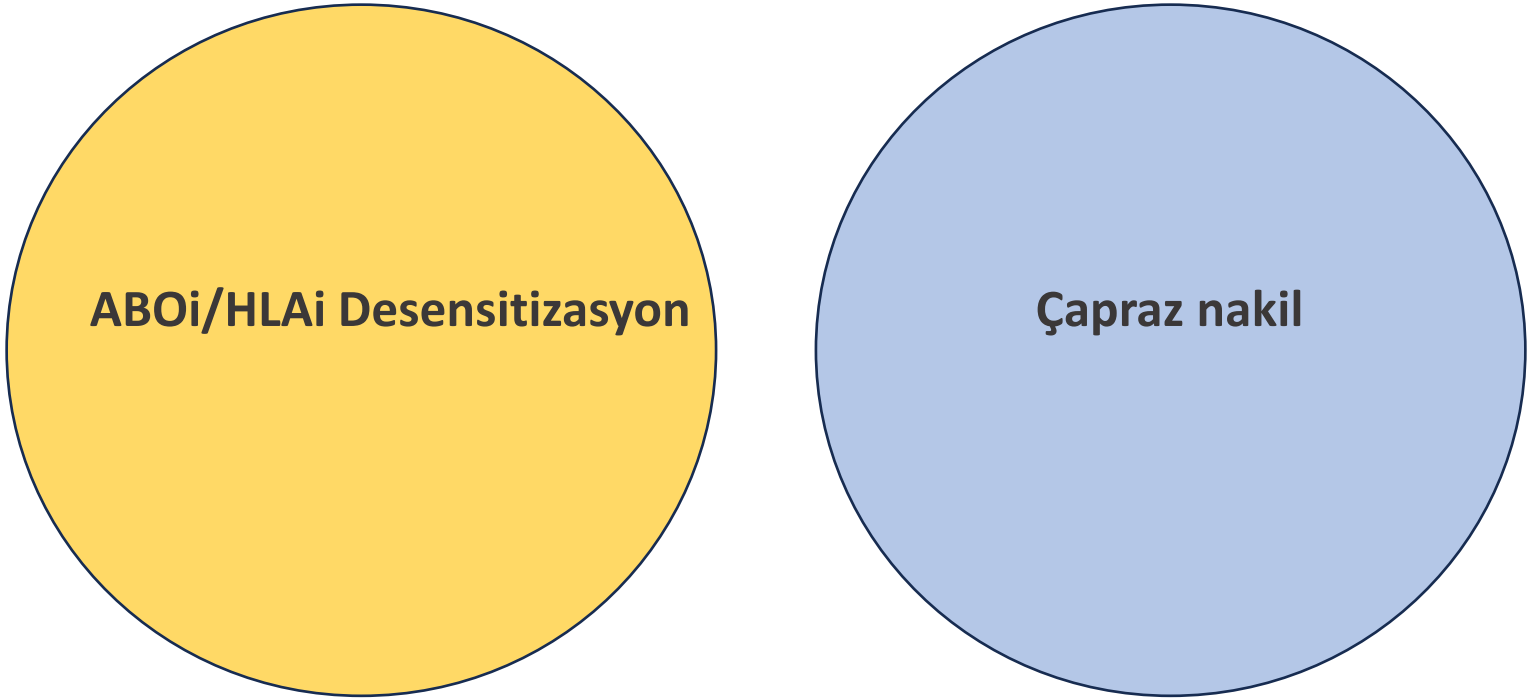
Table 1: Detection of HLA antibodies using different test techniques in patients on the kidney transplant waiting list

	Positive patients							
		ELISA				SAB		
	CDC	Class I	Class II	Class I or II	ELISA or CDC	Class I	Class II	Class I or II
All patients[1] (n = 534)	28 (5%)	48 (9%)	54 (10%)	73 (14%)	78 (15%)	392 (73%)	246 (46%)	435 (81%)
Without history of immunization (n = 133)	2 (2%)	0 (0%)	1 (1%)	1 (1%)	3 (2%)	93 (70%)	45 (34%)	102 (77%)
With history of immunization (n = 286)	22 (8%)	39 (14%)	47 (16%)	61 (21%)	63 (22%)	221 (77%)	150 (52%)	240 (84%)





Riskli Hastalarda Çözümler



Desensitisation

World English Dictionary

desensitize *or* **desensitise** (diː ˈsɛnsɪˌtaɪz)

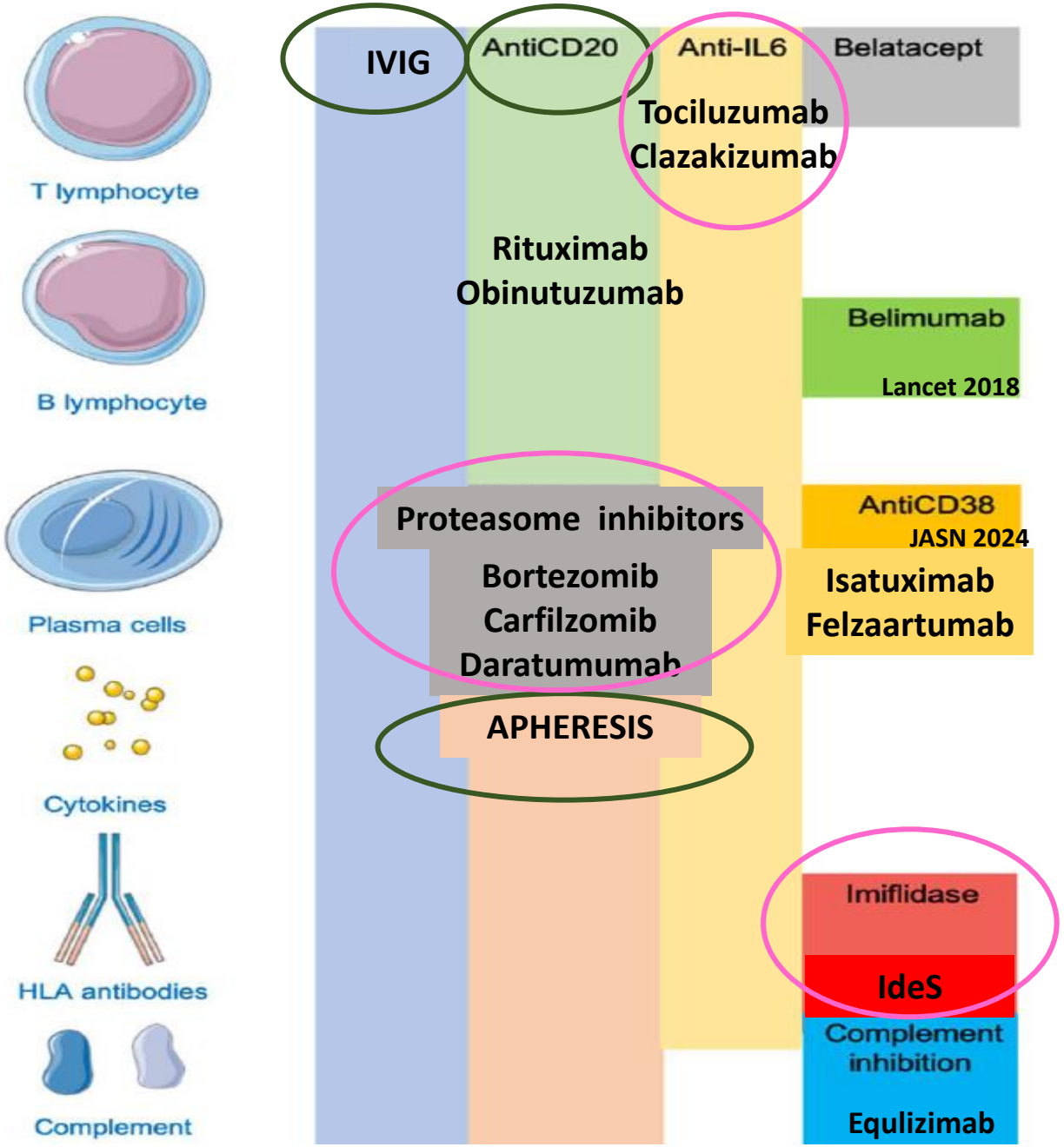
— ***vb***

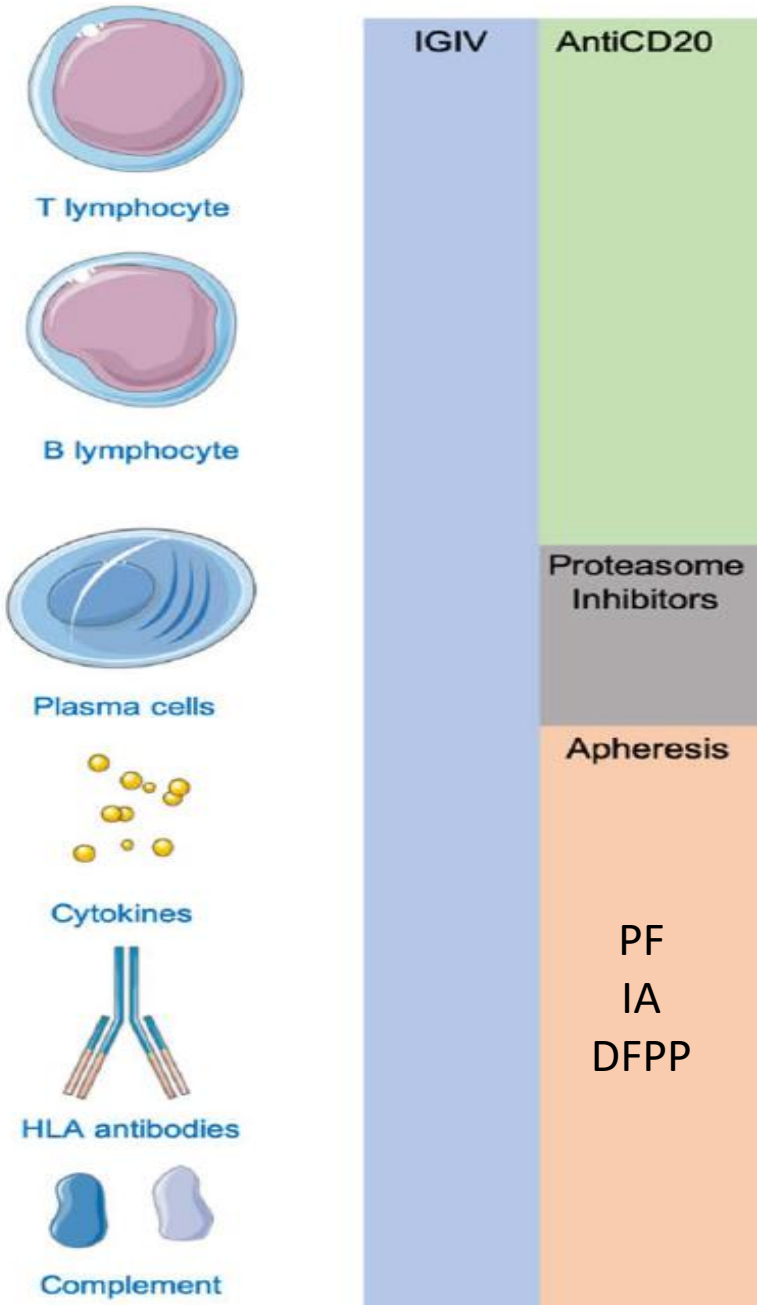
1. to render insensitive or less sensitive: *the patient was desensitized to the allergen ; to desensitize photographic film*
2. *psychol* to decrease the abnormal fear in (a person) of a situation or object, by exposing him to it either in reality or in his imagination

ATG, Steroids

+

Yüksek doz idame 3 lü tedavi





IVIG ve aferez ile, antikor titrelerinde azalma, tx olasılığında artış

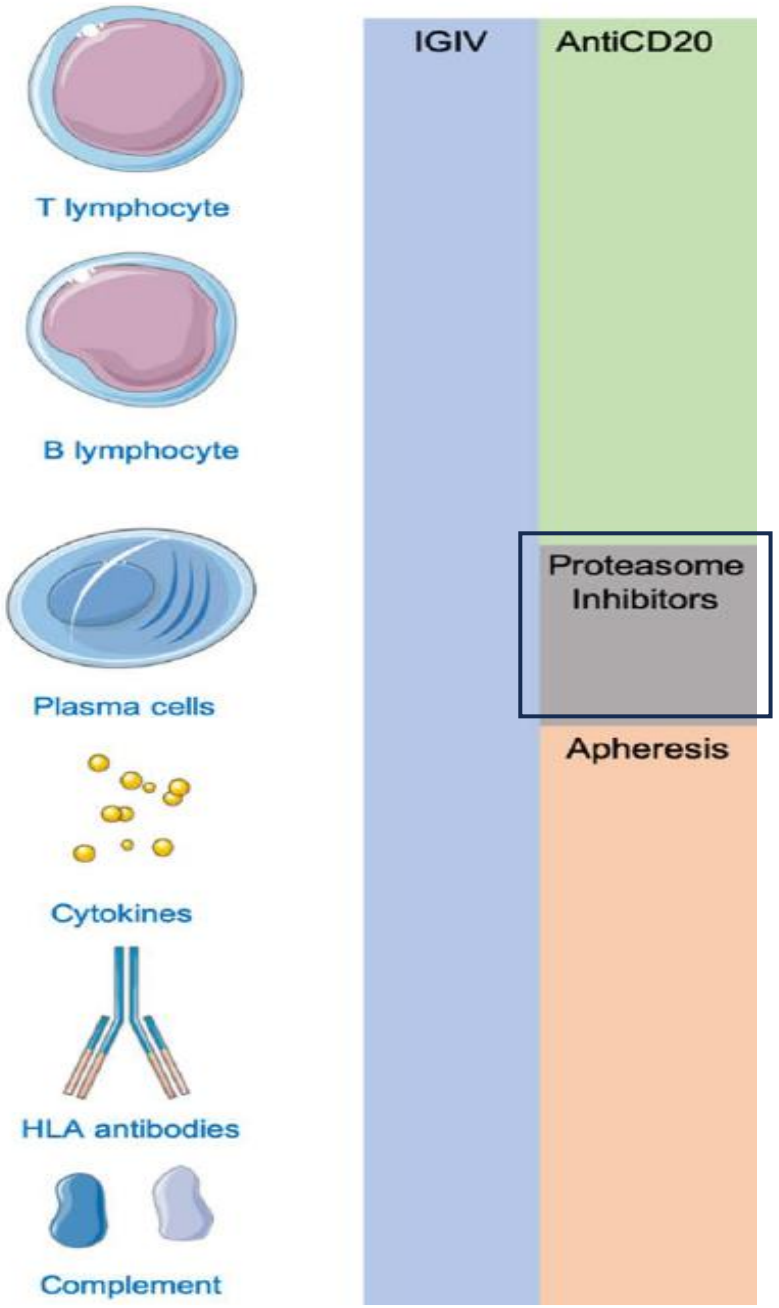
Rituximab ile rebaund ihtimalinde azalma

HD-IVIG grupta negatif CDC XM %36, PE/IVIG/rituximab grup %86

N Engl J Med. 2008, *Kidney Int*. 2015 *Am J Transplant. 2006*

Obinutuzumab, 25 hasta, MFI da azalma, %36 yan etki,ciddi enfeksiyonlar.

Am J Transplant. 2019



Bortezomib, bir çalışmada Anti HLA Ab larda yarıya yakın azalma ve transplantasyon olanağı sağlamış

Prospektif bir çalışmada ise MFI titrsinde azalma sağlasa da cPRAs değişmemiş ve hastaların %20 si y.e nedeni ile ilacı bırakmış.

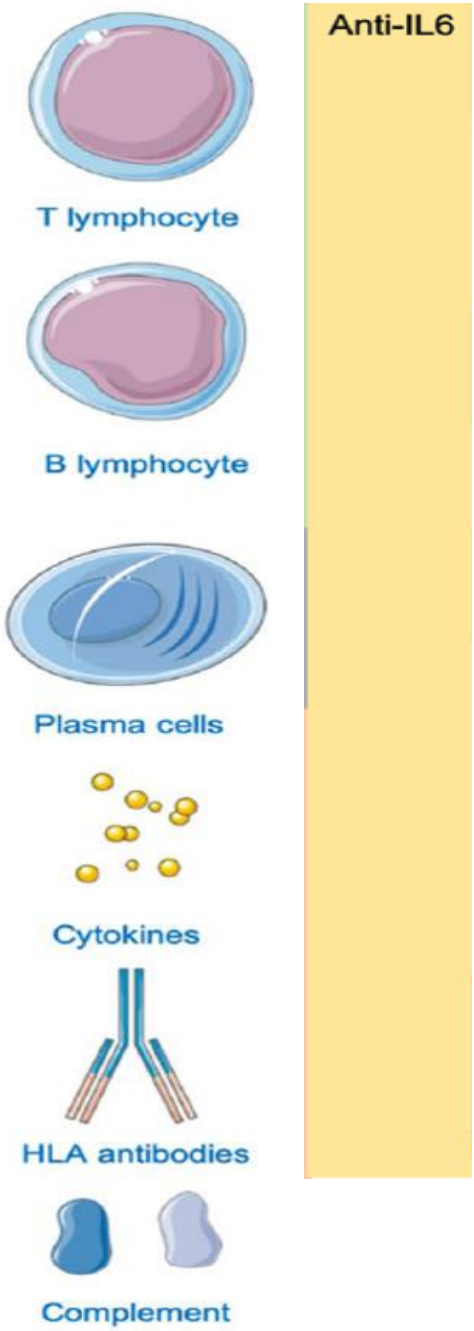
Am J Transplant.2015; Transplantation 2017

Carfilzomib; daha selektif ve daha uzun etkili olduğu iddia ediliyor.

Am J Transplant. 2020

Ixazomib (IXADES), The trial (NCT03213158) enrolled highly sensitized kidney transplant candidates, defined as subjects with calculated panel reactive antibodies (cPRA) >80%, awaiting kidney transplantation >24 months. The subjects were treated with 12 monthly cycles of ixazomib 3 mg+dexamethasone 20 mg. Efficacy was defined as a decrease of cPRA >20% or kidney transplantation.

Kidney360, 2023



Tocilizumab

- ❑ 10 hasta, Anti-HLA Ab da azalma, nakil başarısı %50
- ❑ Ortalama MFI titresinde düşme, B cell matürasyonu aynı
- ❑ Prospektif, 13 hasta, plazmablastlarda anlamlı bir azalma (p = 0,046), Anti-HLA Ab üzerine sınırlı etki
- ❑ TETRA çalışması; standart tedavi (RI+IA) alan 26 hasta ile, ilave TOC alan 7 hasta kıyaslanmış. MFI da azalma veya 1. yıl greft sonuçlarında fark yok

Transplantation 2015, Am J Transplant 2021, Am J Transplant 2022 , J. Clin. Med. 2023

CLlazakizumab

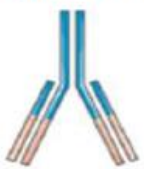
- ❑ PF+IVIG ile birlikte.
- ❑ 20 hastanın 18 inde Anti HLA Ab azalma ve rebaundsuz tx imkanı. Posttx Treg ve Breg artışı

T lymphocyte

B lymphocyte

Plasma cells

Cytokines



HLA antibodies

Complement

Imlifidase desensitization in HLA-incompatible kidney transplantation: finding the sweet spot.

Imlifidase is labeled in Europe for desensitization in HLA-incompatible deceased donor kidney transplantation.

35-kDA cysteine protease from *Streptococcus pyogenes*

cleaves all 4 subclasses of IgG in $F(ab')_2$ and Fc fragments

abrogates IgG - dependent cytotoxicity

- preclinical studies: IgG anti-IdeS antibodies hinder repeated dosing 
- phase II trials:  n=39 FACS+ transplant recipients with 3-year follow-up, 38% ABMR
- phase III: randomized-controlled study enrolling in USA
  post-approval efficacy study enrolling in Europe 
- clinical implementation:

- Identify patients with negligible chances of HLA-compatible donor
- Delist HLA-unacceptable antigens, balancing the risk of rebound
- Mind crossmatching: single cleaved IgG causes FACS/Luminex positive signal.

Imlifidase rapidly and effectively cleaves IgG and prevents hyperacute rejection.
How to combine imlifidase with drugs to dampen DSA rebound will be subject to further studies.

AE de Weerd et al. *Transplantation*. May 2023

@TransplantJrnl

Transplantation

HLAi transplantasyon desensitizasyon sonuçları

Hasta ve greft sağkalımı

	Country	Time (years)	Patient survival, %		*p*-value
			HLAi transplant	No transplant, but on waiting list	
Montgomery, NEJM 2011	United States	8	80.6% *n* = 211	30.5% *n* = 1,050	$p < 0.001$[a]
Orandi, Am J Trans 2014	United States	8	76.5% *n* = 1,025	43.9% *n* = 5,125	$p < 0.001$[a]
Manook, Lancet 2017	United Kingdom	7	78.3% *n* = 213	76.9% *n* = 852	p = NS[b]
Koo, Kidney Int 2021	Korea	7	96.3% *n* = 189[c]	88.2% *n* = 930	$p < 0.001$

Rtx/HD IVIG rejimi, 20 hasta. PRA %77 -%44 e düşmüş. Hasta ve greft sağkalımı 1 yılda %100-94. AR %50, AMR %30

Benzer protokol 76 hasta, **%30 AMR. 2yılda hasta ve greft saağkalımı %95-84**.

NEJM 2008, Transplantation 2010

HLAi transplantasyon desensitizasyon sonuçları

HLAi nakillerde ilk yıl hospitalizasyon ihtimali daha yüksek (RR 5.86; $p < 0.001$), 3.yılda ise düşük (RR 0.74, $p < 0.001$).

56 HLAi ile 274 HLAc nakil enfeksiyon riskleri açısından karşılaştırılmış.
UE (41% vs. 7.7%), CMV viraemia (54% vs. 14%) ,pneumocystis jiroveci pneumonia (PJP) (5% vs. 0%) ($p < 0.001$).

Orandi, Am J Trans 2014, BMC Nephrol (2019)

Erken ve geç dönem enfeksiyonlar, viral reaktivasyonlar, İnfüzyon reaksiyonları
Koagülopati, kateter komplikasyon, elektrolit bozuklukları

Transplant Proc 2023 Sep

Postoperative Events in Incompatible Living Donor Kidney Transplant Recipients Undergoing Prior Desensitization

This study aims to analyze the **surgical complications and bleeding events** presented in ABO-incompatible (ABOi) and HLA-incompatible (HLAi) patients within a **pre-transplant desensitization program** compared with ABO-compatible (ABOc) recipients.
We found a greater **number of postoperative surgical complications when analyzing the number of hematomas, size, need for surgical reintervention, and the number of blood units transfused**; incompatible patients showed higher rates of hematomas, need for surgical reinterventions, and transfused units ($P < .05$).

viruses

MDPI

Article

Impact of B Cell Depletion on COVID-19 in Kidney Transplant Recipients

Viruses **2023**

Abstract: Kidney transplant recipients are patients at high risk for coronavirus disease 2019 (COVID-19) due to being on immunosuppressive therapy. B cell depletion therapy, including rituximab, is an important strategy for ABOi transplants. However, knowledge about the effect of B cell depletion therapy on COVID-19 is lacking. Thirty kidney transplant recipients who developed COVID-19 were included in this study. To examine the impact of B cell depletion therapy, we retrospectively investigated the relationship between the background of the patients and the clinical outcome. **Of the 30 patients, 13 received B cell depletion therapy**. The median time between transplant and onset of COVID-19 was **6.1 years** after transplantation; however, nine cases remained markedly depleted of **CD19(+) cells (<4.0%).** The patients were assigned to the normal (n = 21) and depletion groups (n = 9). Progression rates in the depletion and normal groups were 55.6% and 9.5%, respectively (p = 0.014). Furthermore, the survival rate was significantly lower in the depletion group (100% in the normal group vs. 66.7% in the depletion group; p = 0.021). **B cell depletion therapy may have long-term effects and increase the risk of COVID-19 in kidney transplant recipients.**

How safe is crossing the ABO blood group barrier in kidney transplantation?

CJASN
Clinical Journal of American Society of Nephrology

Meta-analysis

26 single-center studies

ABO incompatible kidney transplants + same center controls

	1 yr graft survival	Infectious cause of death	Antibody mediated rejection	Non-viral infection
ABO Compatible (N=4943)	98%	13%	2%	6%
ABO Incompatible (N=1346)	96%	49%	10%	12%
	p<0.001	p=0.02	p<0.001	p=0.005

Conclusions ABO-incompatible kidney transplant recipients have good outcomes albeit inferior to center-matched ABO-compatible control patients

Annelies E. de Weerd and Michiel G.H. Betjes. ABO-Incompatible Kidney Transplant Outcomes: A Meta-Analysis. CJASN doi: 10.2215/CJN.00540118

Clinical outcomes after ABO-incompatible renal transplantation: a systematic review and meta-analysis

www.thelancet.com, 2019

Findings 1264 studies were screened and 40 studies including 49 patient groups were identified. 65 063 patients were eligible for analysis, 7098 of whom had undergone ABOi-rTx. Compared with ABOc-rTx, ABOi-rTx was associated with significantly higher 1-year mortality (odds ratio [OR] 2·17 [95% CI 1·63–2·90], p<0·0001; I^2=37%), 3 years (OR 1·89 [1·46–2·45], p<0·0001; I^2=29%), and 5 years (OR 1·47 [1·08–2·00], p=0·010; I^2=68%) following transplantation. Death-censored graft survival was lower with ABOi-rTx than with ABOc-rTx at 1 year (OR 2·52 [1·80–3·54], p<0·0001; I^2=61%) and 3 years (OR 1·59 [1·15–2·18], p=0·0040; I^2=58%) only. Graft losses were equivalent to that of ABOc-rTx after 5 years and patient survival after 8 years. No publication bias was detected and the results were robust to trial sequential analysis until 5 years after transplantation; thereafter, data became futile or inconclusive.

Interpretation Despite progress in desensitisation protocols and optimisation of ABOi-rTx procedures, excess mortality and loss of kidney grafts was found compared with ABOc-rTx within the first 3 years after transplantation. Only long-term outcomes after 5 years yielded equivalent survival rates and organ function. Awareness of the increased risks of infection, organ rejection, and bleeding could improve care of patients and promote efforts towards paired kidney exchange programmes.

1 yıllık mortalitede 2.17 kat ,3 yıllık mortalitede 1.89 ve 5 yılda 1.47 kat artış.
Greft kaybı 5 yıl, hasta kaybı 8 yıl sonra ABOc ile benzer.

Transplant Direct, 2022 Oct
Patient and Graft Survival After A1/A2-incompatible Living Donor Kidney Transplantation

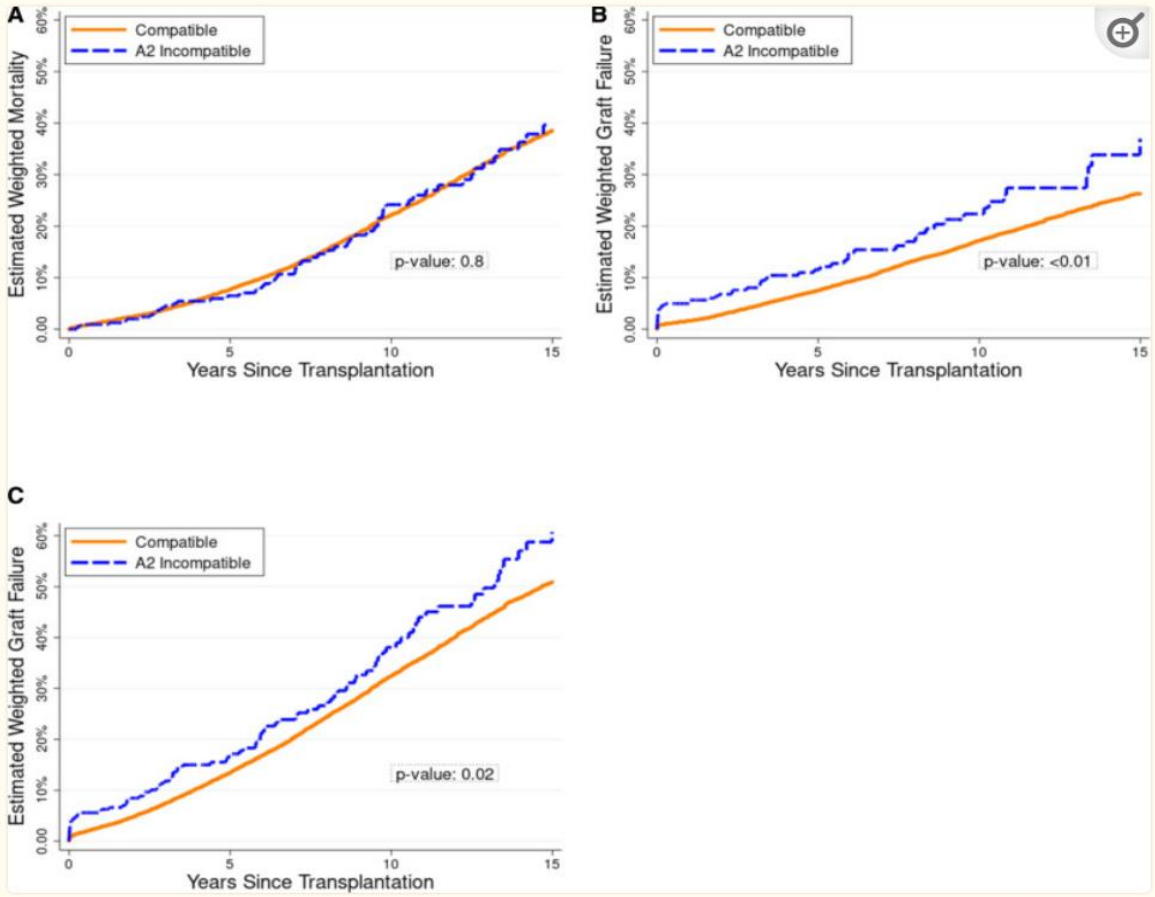


FIGURE 2.

Posttransplant outcomes among A2i vs comparable ABOc LDKT recipients. Estimated weighted cumulative incidence of (A) mortality, (B) death-censored graft failure, and (C) all-cause graft loss after kidney transplant among patients who received an A2i or ABOc LDKT. A2i, A2-incompatible; ABOc, ABO-compatible; LDKT, living donor kidney transplantation.

Am J Transplant ,2024 Apr
A2/A2B to B deceased donor kidney transplantation in the Kidney Allocation System era

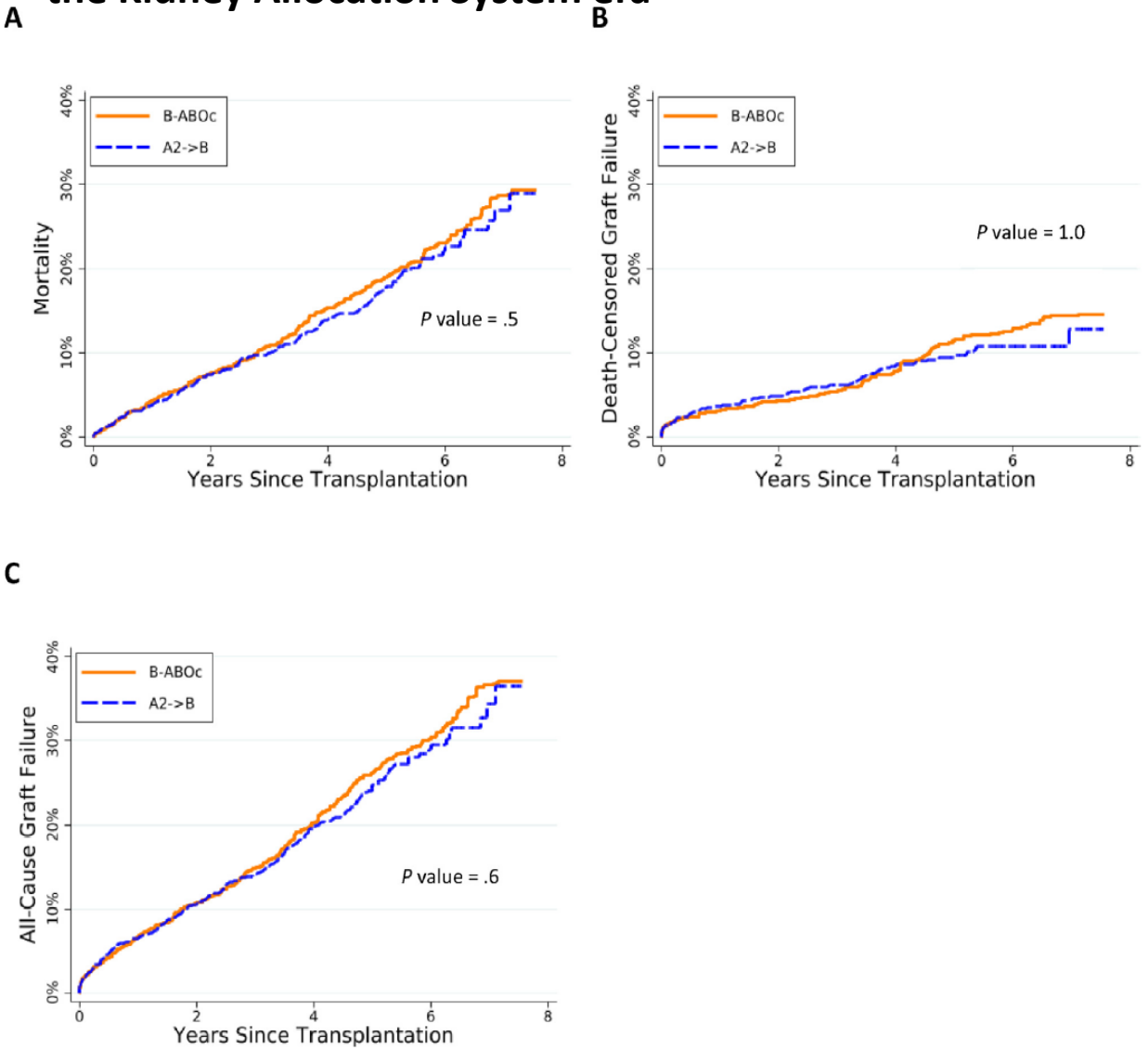


Figure 4. Weighted estimate of the cumulative incidence of (A) mortality, (B) death-censored graft failure, and (C) all-cause graft loss after kidney transplant among patients who received an A2→B or comparable ABO-compatible (B-ABOc) deceased donor kidney transplant.

A multicenter retrospective cohort study on management protocols and clinical outcomes after ABO incompatible kidney transplantation in India

Methods

- Retrospective analysis
- India
- 5 March'11- 2 July 2022
- Multicenter (25 centres)
- 1759 LKT ABOi and 33,157 ABO-cKT

Protocol

Rituximab
100 mg :13.18%
200 mg : 49.85%
500 mg: 32.34%

No induction
11.37%

IVIG
37.69%

IA
8.24%

Findings

Mortality	Graft Loss	BPAR	Infection
9.49%	7.73%	12.96%	17.39%

Median follow-up of 36.3 months

Higher with IA , BPAR, Graft loss

Higher with IA and conventional tube method

Improved graft survival with IVIG
HR:0.44 (0.26-0.72);
p =0.0010

No impact on primary outcome
Rituximab dosing
High pre-conditioning/
Pre-surgery Anti-A/ Anti-B titers

In unmatched univariate analysis, the outcomes between ABOiKT and ABOcKT were comparable

ABOi: ABO incompatible kidney transplantation LKT: Living kidney transplantation, IVIG: , IA: Intravenous immune globulin, IA: Immunoadsorption, BPAR: biopsy-proven acute rejection

Conclusion: The largest multicenter study on ABOiKT provides insights into various protocols and management strategies with results comparable to those of ABOcKT

Kute V et al. 2023
Visual Abstract by Priti Meena, MD.
@TransplantJrnl

Transplantation

Kıyaslama verisi

Impact of ABO-Incompatible Living Donor Kidney Transplantation on Patient Survival

808 ABOi hasta ile USA deki SRTR listresinden match control 2423 hasta seçilerek karşılaştırlmış. İlk 30 gün mortalite yüksek, 180 günden sonra daha düşük bulunmuş. *Am J Kidney Dis . 2020*

27 HLAi hasta 69 ABOi hasta ile karşılaştırlmış, sadece PJP farklı (%6-0) *Transpl Int (2015)*

ABO uyumsuz nakiller veya desensitizasyon tedavilerinde EK maliyetler

- İmmunadsorbsiyon seans = 16.000 TL.

- Plazmaferez seans +alb ile= 7942+(6x2220) =21.262 TL
- Plazmaferez seans+ TDP ile =7942+(10x425)=12.200 TL

- Rituximab 500 mg flakon =20.000 TL

- Yatış, reop. vb diğer maliyetler

Çapraz nakil (Kidney paired donation (KPD),Paired kidney Exchange (PKE), Paired Living Kidney Donation

- İlk olarak **Rapaport tarafından 1986** da tanımlanmıştır.
- İlk kez 1991 de Güney Kore'de gerçekleştirilmiştir.
- 2000'lerden sonra birçok Avrupa ülkesi ve ABD de önce yerel sonra geniş çaplı veya ulusal sistemler başlamış
- **İlk ulusal çapraz nakil havuzu 2005 de Hollanda'da oluşturulmuştur.**

İmmunolojik Alt Yapı

13.5 OPTN KPD Histocompatibility Testing

13.5.A HLA Typing Requirements for OPTN KPD Candidates

HLA-A HLA-B HLA-Bw4 HLA-Bw6 HLA-DR
Eğer hastada listelenen HLA tiplerine karşı bir unacceptible antigen varsa, **split düzeyinde HLA** sonuçlarını da içermelidir.

HLA-C HLA-DR51 HLA-DR52 HLA-DR53 HLA-DPB1 HLA-DQA1 HLA-DQB1

13.5.C HLA Typing Requirements for OPTN KPD Donors

HLA-A HLA-B HLA-Bw4 HLA-Bw6 HLA-C HLA-DR HLA-DR51 HLA-DR52 HLA-DR53 HLA-DQA1 HLA-DQB1 HLA-DPB1

İmmunolojik Alt Yapı

Enrolment and Medical Evaluation

Immunology data entered into OrganMatch

Donors must have an authorised HLA typing at **4-digit level** recorded into OrganMatch for each of the following mandatory HLA loci:

HLA-A*, HLA-B*, HLA-Cw*, HLA-DRB1*, HLA-DQB1*, HLA-DQA1*, HLA-DPB1* and HLA-DRB3/4/5*.

Sensitised recipients must have an authorised Class I and Class II HLA antibodies by solid phase single antigen bead assays (Luminex) at **4-digit level** recorded into the OrganMatch. DSA with MFI>2000 (One Lambda) or >1500 (Immucor) excludes from matching.

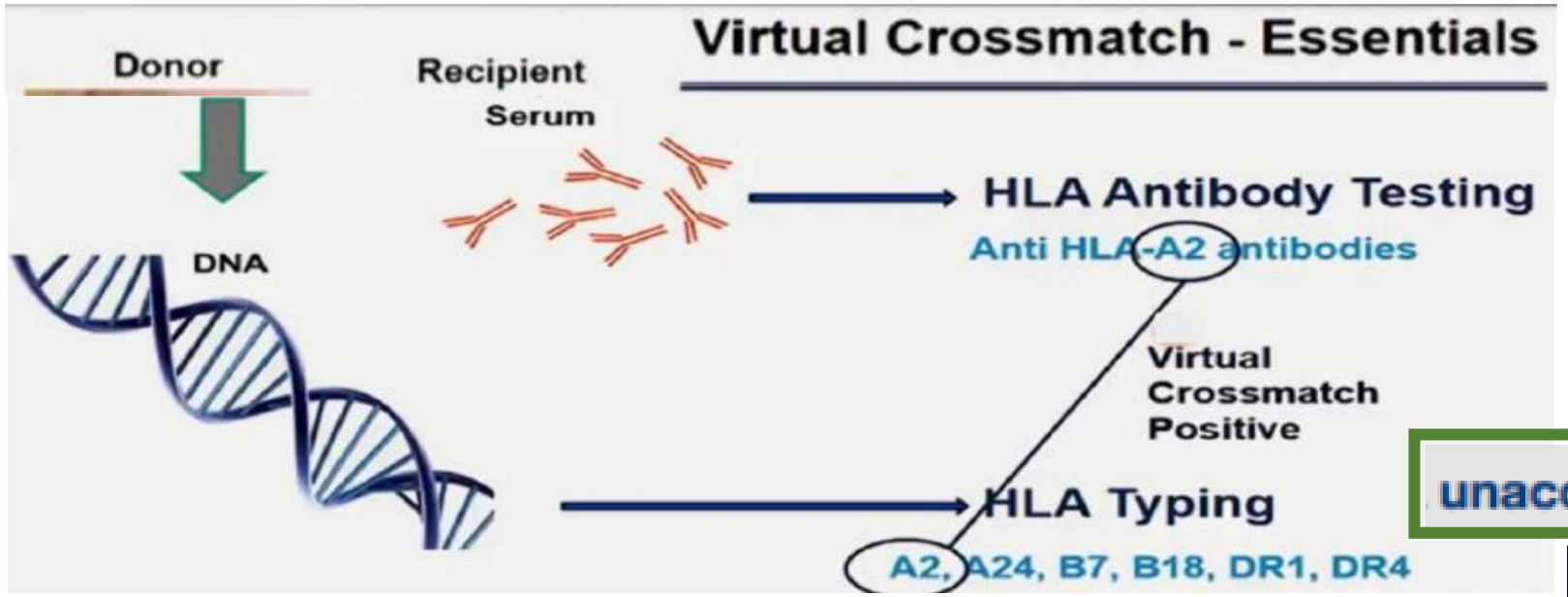
Examples:	2 field molecular	1 field molecular	Serological
	A*11:01	A*11	A11
	C*03:04	C*03	Cw10
	DRB1*03:01	DRB1*03	DR17

İmmunolojik Alt Yapı

Table 1. ABO and immunological data recorded in KEP by various countries.

	Australia	Scandinavia	UK	Switzerland	Spain	Italy	Belgium	Netherlands	Portugal
Blood group of donor and recipient	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Recipient's acceptance of ABOi donor	Yes	Yes	Yes	Yes	Yes	No	No	No	No
HLA donor typing and recipient HLA antibody	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Resolution	High	High	High and low	Low, high upon request	High and low	High	Low	High and low	Low
A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
B	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
C	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
DRB1	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
DQB1	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
DQA1	Yes	Yes	No	No	No	Yes	Yes	No	No
DPB1	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No
DPA1	Yes	Yes	No	No	No	Yes	No	No	No
DRB3/4/5	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No

Virtual Crossmatch



unacceptable antigen

UNOS

Patient:

A1, A30; B7, B8 ; DR11, 15; DQ6, 7

Antibodies - DR7, DR9, DR53, DQ2

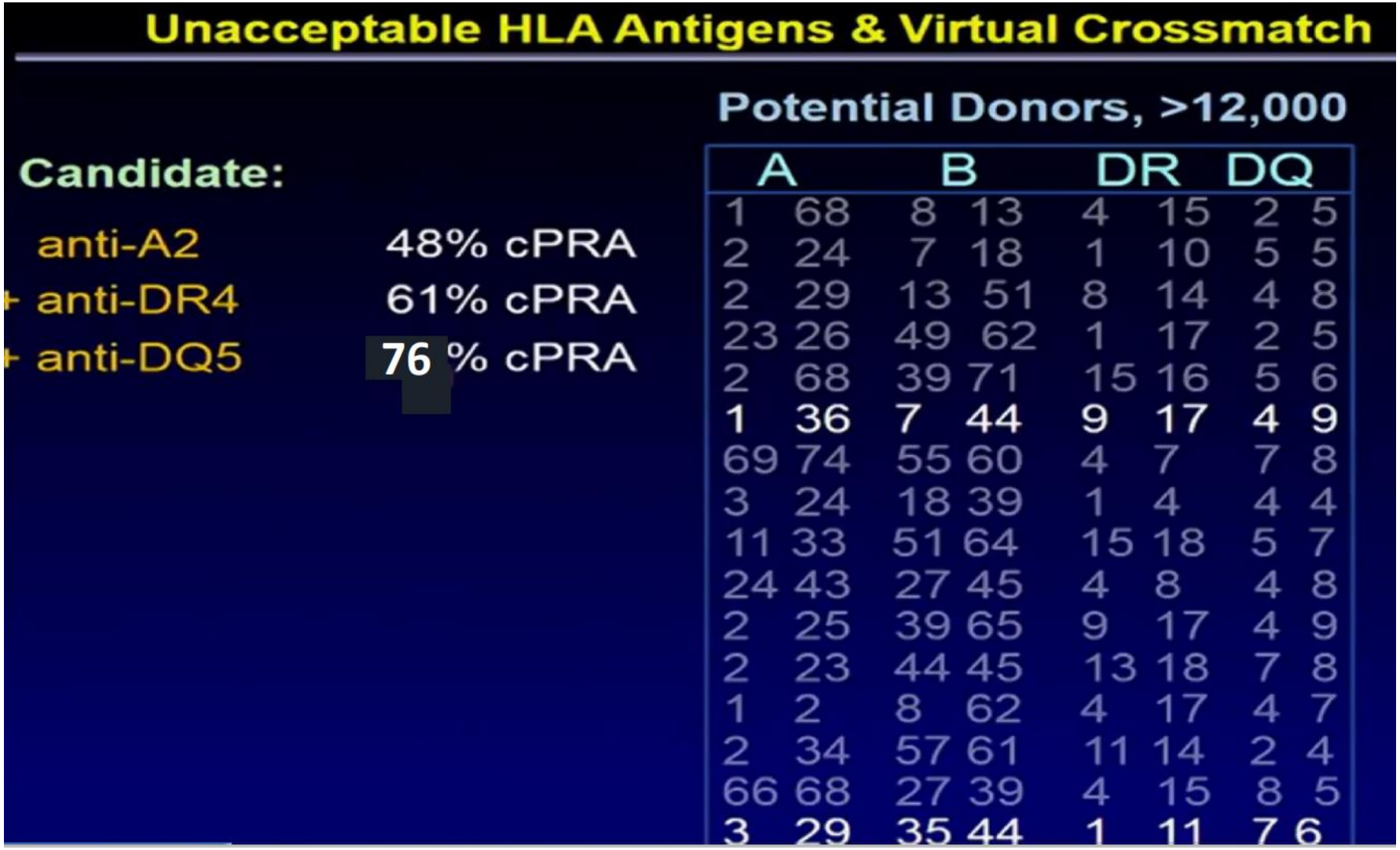
Potential Donor: complete mismatch

A25, A33; B42, B18; DR8, DR16; DQ4, DQ5

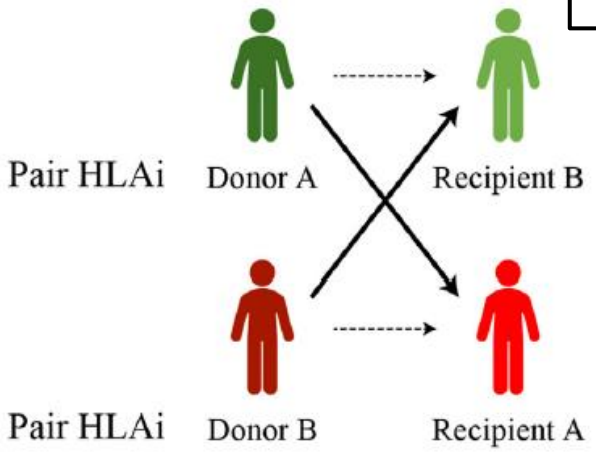
Acceptable Mismatches (AMm)

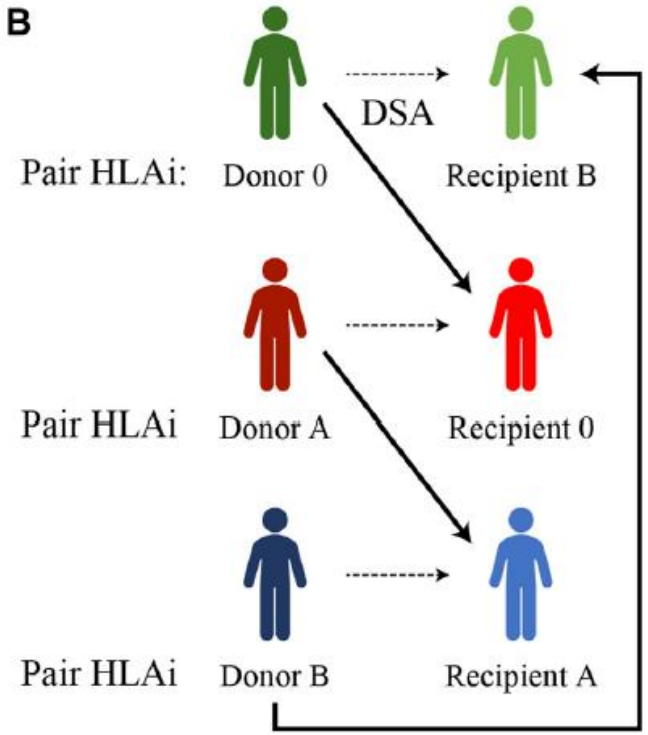
Eurotransplant

cPRA (Calculated PRA)



Çapraz Nakil Modelleri





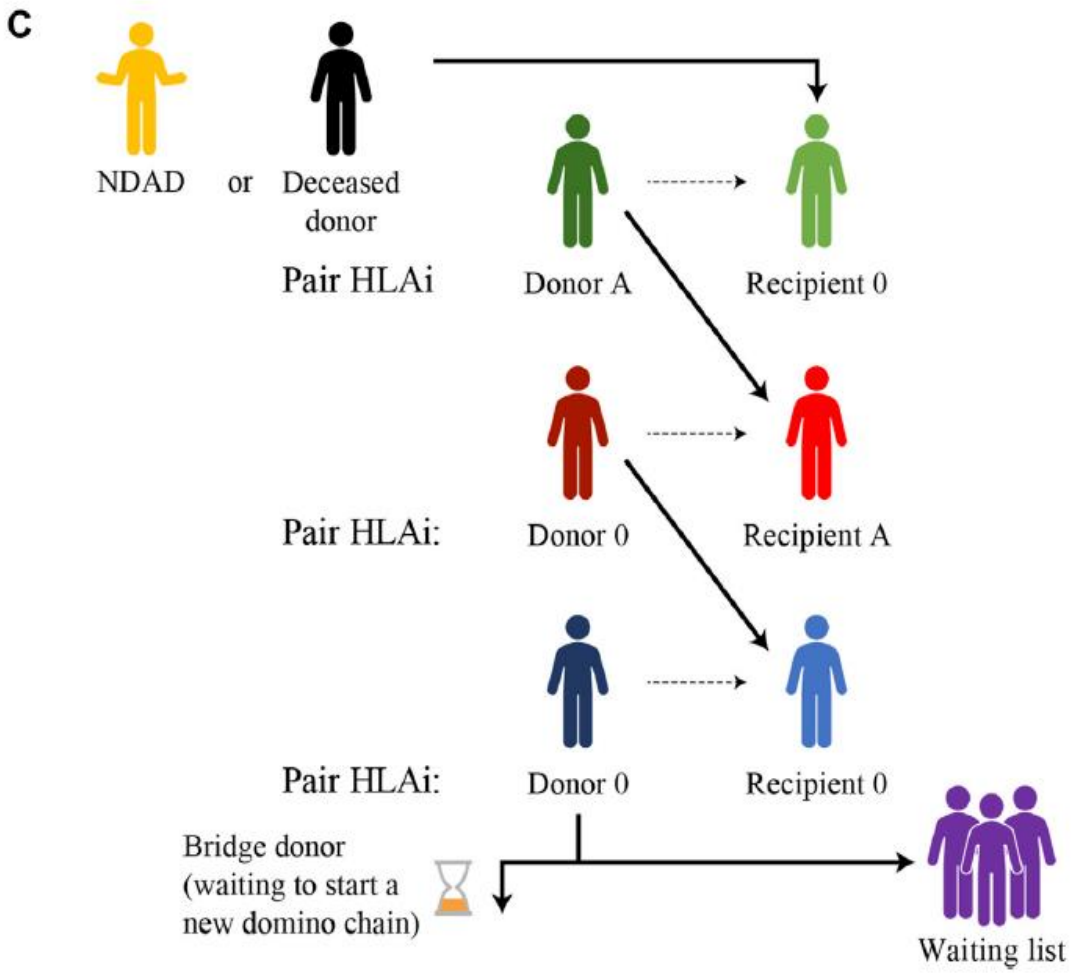
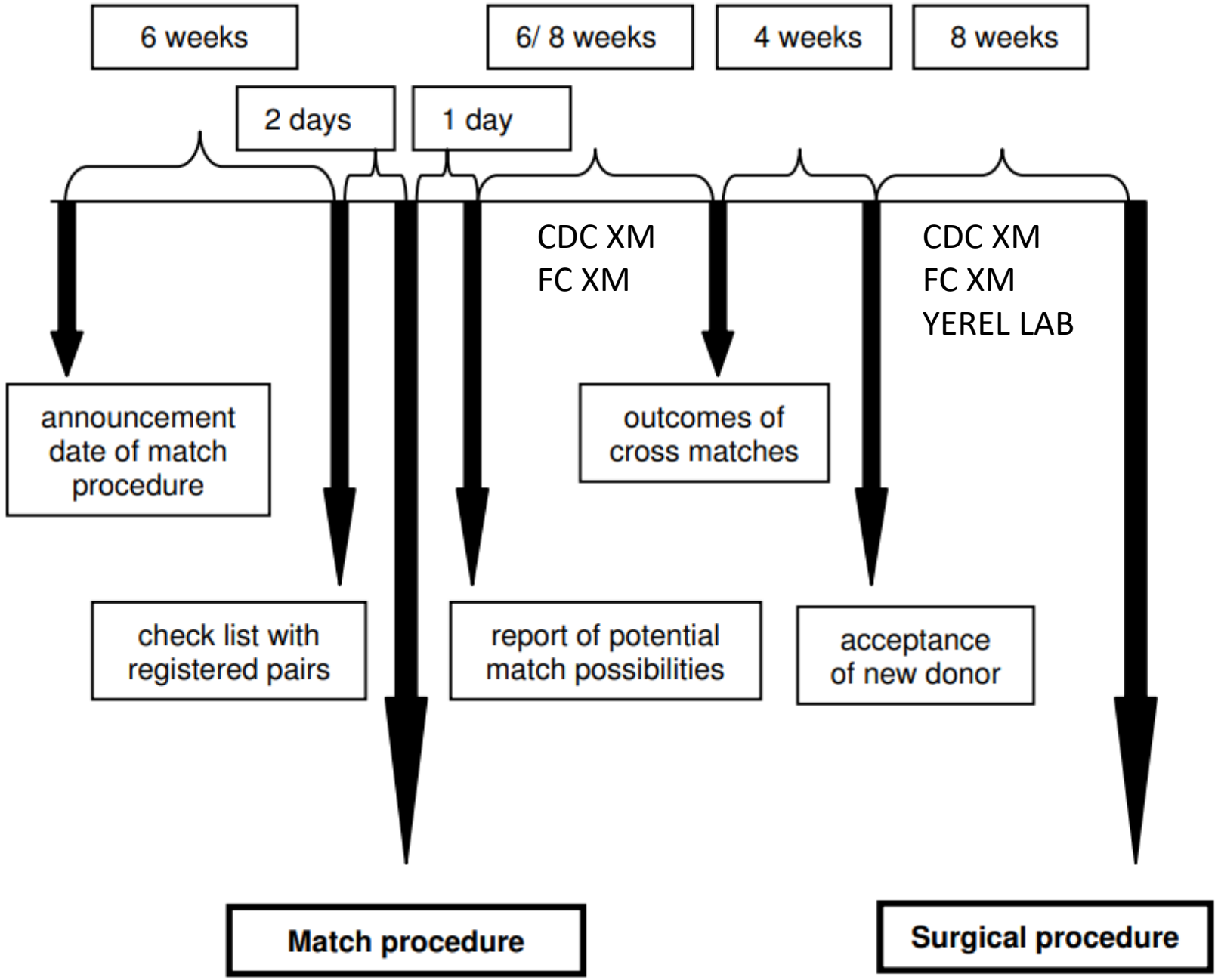


FIGURE 1 | Examples of kidney paired donation exchanges **(A)** Two-way exchange **(B)** Three-way exchange **(C)** Domino-chain ending with a donation to a wait-list patient or a bridge donor and starting from a non-directed altruistic donor (NDAD), a non-simultaneous extended altruistic donor (NEAD), or a deceased donor (Dec-K program).

Table 1. Key ingredients of four national kidney paired donation registries

Country	The Netherlands	UK	Canada	Australia	US
Year established	2004	2007	2009	2010	Kidney Paired Donation
Name of program	Living Donor Exchange Programme	National Living Donor Kidney Sharing Scheme (NLDKSS)	Canadian Blood Services Kidney Paired Donation Program (CBS-KPD)	Australian paired Kidney eXchange Program (AKX)	National registry and smaller independent registries exist
HLA laboratories involved	Single	Multiple	Multiple	Multiple	
Types of exchanges considered	Multiway and domino	Multiway and domino	Multiway and domino	Multiway and domino	Multi way and domino
Accepts ABO-incompatible donor matching	No	Yes	No	Yes	No
Donor allocation algorithm	Virtual cross-match	Virtual cross-match	Virtual cross-match	Virtual cross-match	Unacceptable antigens based on recipient's serological DSA for
Primary allocation criteria	Unacceptable antigens based on recipient's serological DSA for HLA-A, B, Bw, DR, DQ	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQB1, DPB1	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQA1, DQB1, DPA1, DPB1	Negative virtual cross-match at HLA-A, B, C, DRB1, DRB345, DQA1, DQB1, DPA1, DPB1	HLA-A, B, C, DRB1, DRB345, DQA1, DQB1, DPA1, DPB1
Desensitization programme in combination with KPD	No	No	No	Yes	Yes

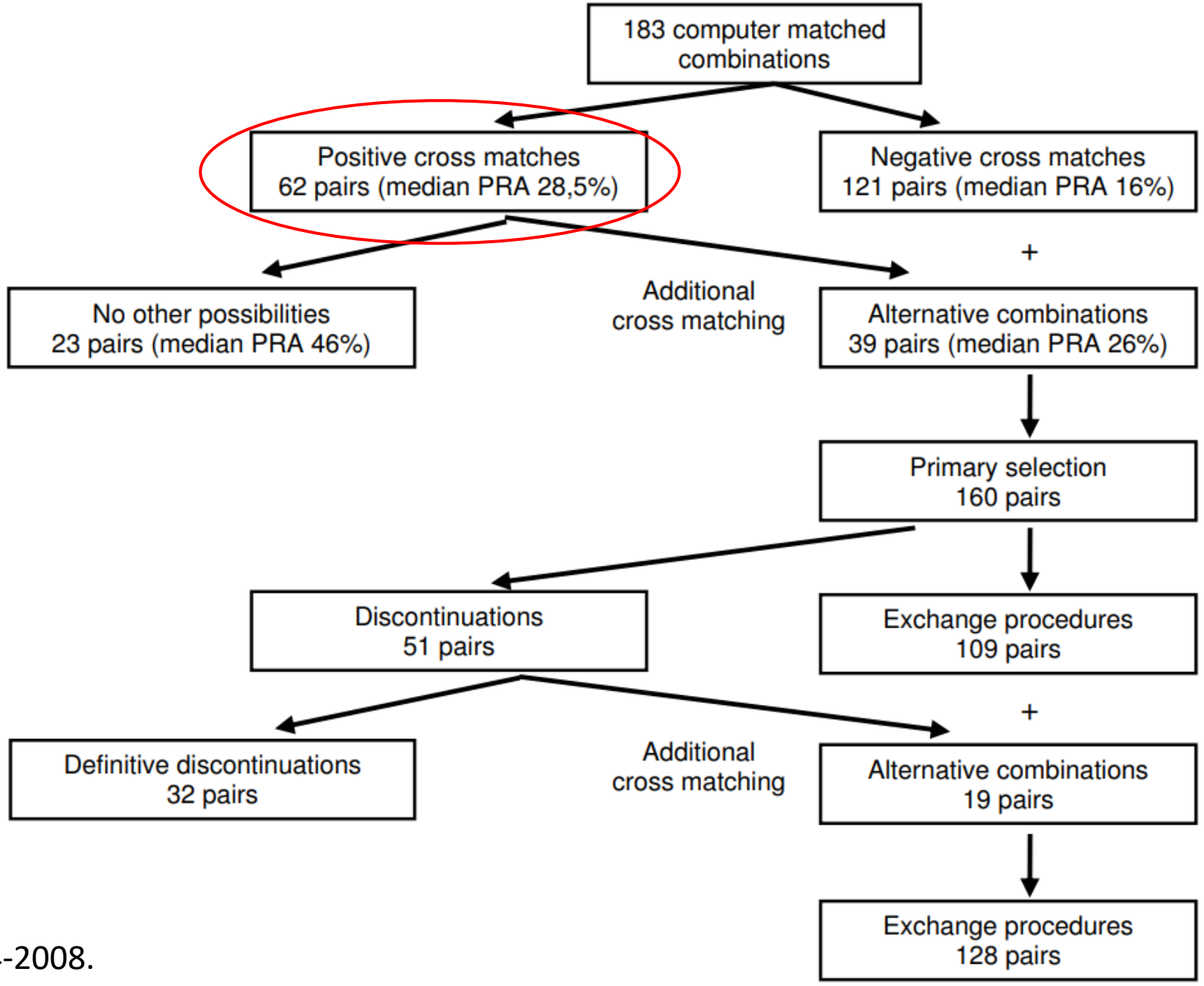


SAB testi girişte çift

Sensitizasyon olasılığı mevcut olay sonrası

Eşleşme gerçekleşti ve test 3 aydan eski ise

XM testi 1 aydan eskiyse tekrar SAB yapılır, değişiklik yoksa yeni XM gerekmez



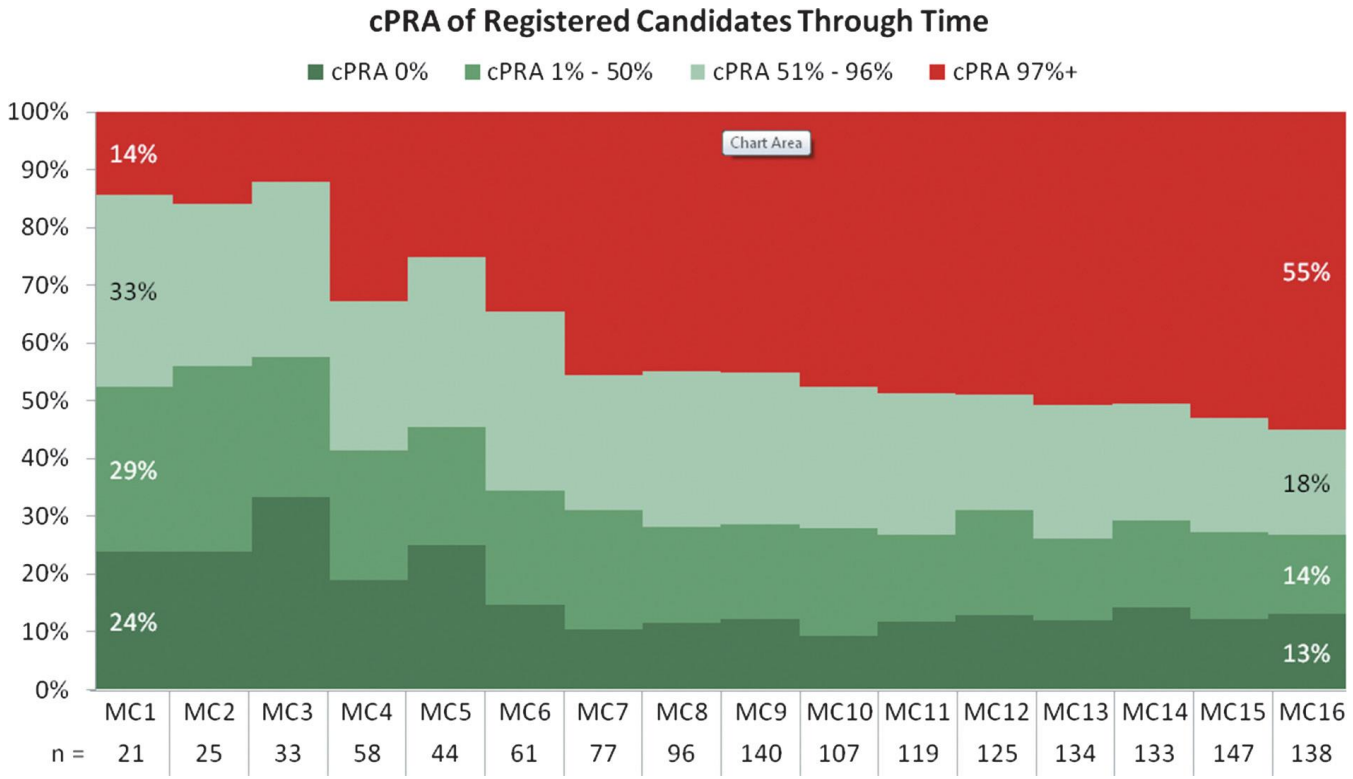
2004-2008.

333 XM
2.6 XM/match

HEDEF → ABO uyumu ve DSA /XM negatif eşleşme

Sensitize hastalar puantaj sisteminde öne çıkarılmalı

cPRA kullanımı



Başlangıç eşleşme kriterleri daha geniş tutulabilir.

Uyum yerine uyumsuzluk ön plana çıkarılması---Unacceptible Mismatch.

Unbalanced KPD---Uyumlu çiftlerin alınması

Düşük titre antikorlu ABOi

EUROSTAM

Virtual Crossmatch Approach to Maximize Matching in Paired Kidney Donation

American Journal of Transplantation 2011;

Table 2: Comparison of 3 test runs using different antibody resolution and strength to exclude recipients with antibodies from matching to donors in a pool of 32 incompatible donor recipient pairs

	Run 1	Run 2	Run 3
	Low Resolution MFI > 8000	High Resolution MFI > 8000	High Resolution MFI > 2000
Time to match	3h 45 min	3h 58 min	0h 50 min
No. of matched pairs	439	445	355
No. of chains	308	316	191
No. of combinations	22 703	24 113	8843
No. of patients in 1st combination	20	19	17
3-way chains in 1st combination	4	5	5
2-way chains in 1st combination	4	2	1
Recipients with DSA 2000–8000MFI	6	4	0
No. of patients in chains with predicted negative crossmatch	8	10	17
Donor/Recipient age difference (years)	0.9 ± 14.2 (–24 to 24)	1.2 ± 13.6 (–25 to 29)	4.0 ± 14.7 (–24 to 29)

Table 3: Match results by blood type excluding recipients with donor specific antibody at >2000 mean fluorescence intensity (One Lambda) and using high-resolution antibody definition

Blood type incompatible pairs (N = 16)			Crossmatch positive pairs (N = 16)		
Blood group donor → recipient	No. in pool	matched	Blood group donor → recipient	No. in pool	matched
A → O	11	3	O → O	5	2
B → O	2	1	O → A	7	7
AB → O	1	0	A → A	3	2
A → B	2	1	B → AB	1	0
31% match rate (5/16)			**75% match rate (12/16)**		

Table 2. Outcomes of various paired kidney exchange studies.

Author and year	Sample	Outcome	Remarks
Leeser et al. 2020 [16] (2008–2017) *NKR, USA*	2363 NKR PKE compared to control kidney transplant recipients (n = 54,497)	Median follow-up 3.7 years Similar graft failure and mortality	NKR registry was relatively high risk – more likely to be black, women, older, >80% PRA, previous transplant and
Flechner et al. 2018 [22] *NKR, USA*	Tuncer et al. 2012 [72] (2008–2011) *Turkey*	57 PKE vs. 1081 living related txp	Similar first and second year GFR, AR, graft loss, pt. loss	PKE pts had higher HLA mismatch and age
	Leeser et al. 2012 [73] (2007–2011) *NKR, USA*	44 pair leading to 50 txp.	DGF – 6%; 1 year rejection rate – 9.1%; 1 year pt. and graft survival 98% and 94%	Blood type incompatibility – 54.4%; sensitization – 43.2%
Allen et al. 2018 [69] *Australia*	Bingaman et al. 2012 [19] (3 years) *Methodist San Antonio, USA*	134 (117 incompatible and 17 compatible pairs)	3 episodes of rejection, no graft lost due to rejection	5 desensitization combined with PKE 44% with PRA >80%
Kute *et al.* 2017 [70] (2000–2016) *India*	Klerk et al. 2011 [74] (2004–2011) *Dutch PKE program*	187 transplants – 83 blood group incompatible and 104 positive crossmatch pairs	5-year uncensored survival – 85%; death censored graft survival – 89%	40% of the registered patients got transplanted
Jha et al. 2015 [71] (2010–2013) *India*				
Malik et al. 2014 [12] (2009–2013) *Canada*	Montgomery et al. 2005 [18] (2001–2004) *Johns Hopkins, USA*	22; median follow-up 13 months	Patient survival 100%; graft survival 95.5%; 6 months creatinine – 1.2 mg/dl; ACR – 18%; no AMRs	Two triple exchanges; 5 patients were highly sensitized

Massie AB, et al. A Risk Index for Living Donor Kidney Transplantation *Am J Transplant. 2016*

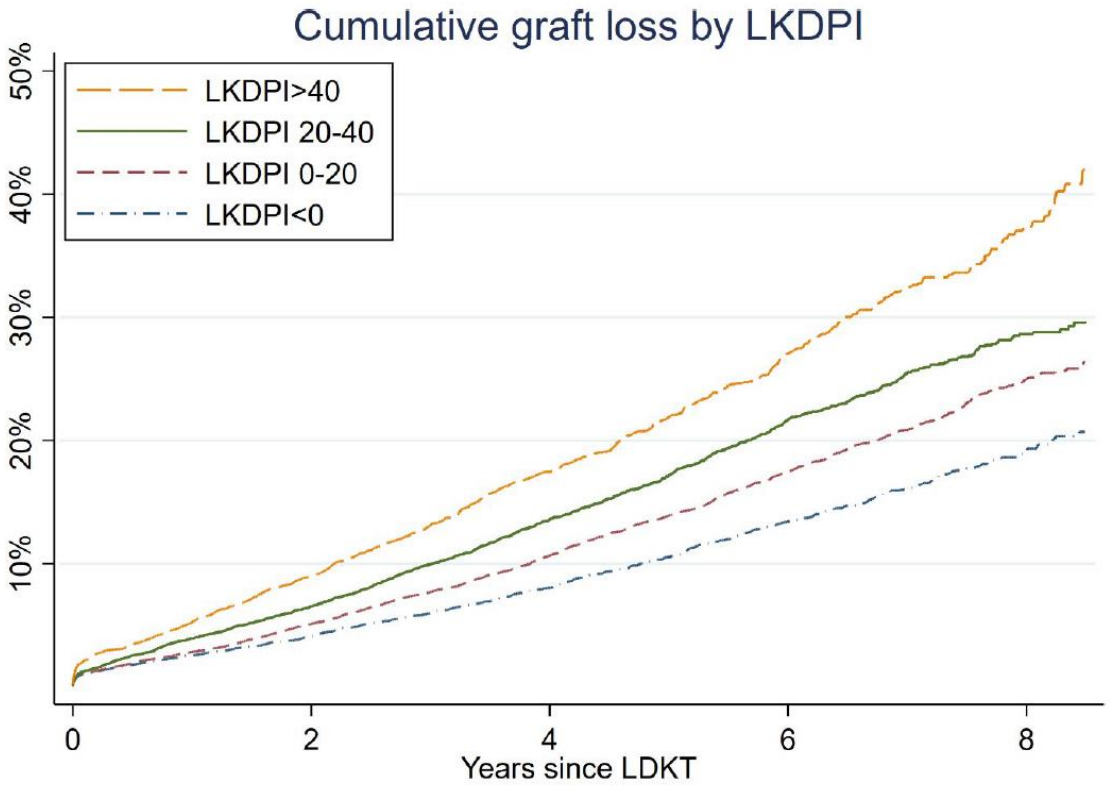


TABLE 1 Components of the living kidney donor profile index (LKDPI)

Component	Points
	−11.30
Age > 50	+1.85 × (age−50)
Estimated glomerular filtration rate (eGFR)	−0.38 × eGFR
Body mass index (BMI)	+1.17 × BMI
Donor/recipient male gender	+1.17
African-American race	+22.34
Donor/recipient ABO incompatible	+27.30
History of cigarette use	+14.33
Systolic blood pressure (SBP)	+0.44 × SBP
Donor/recipient not biologically related	−10.61
HLA-B mismatch	+8.57 × number of mismatches
HLA-DR mismatch	+8.26 × number of mismatches
Donor/recipient weight ratio	−50.87 × (minimum of [donor/recipient weight ratio, 0.9])

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American Journal of Transplantation 23 (2023) 232–238

journal homepage: www.amjtransplant.org

Original Article

The living kidney donor profile index fails to discriminate allograft surv implications for its use in kidney paired donation programs

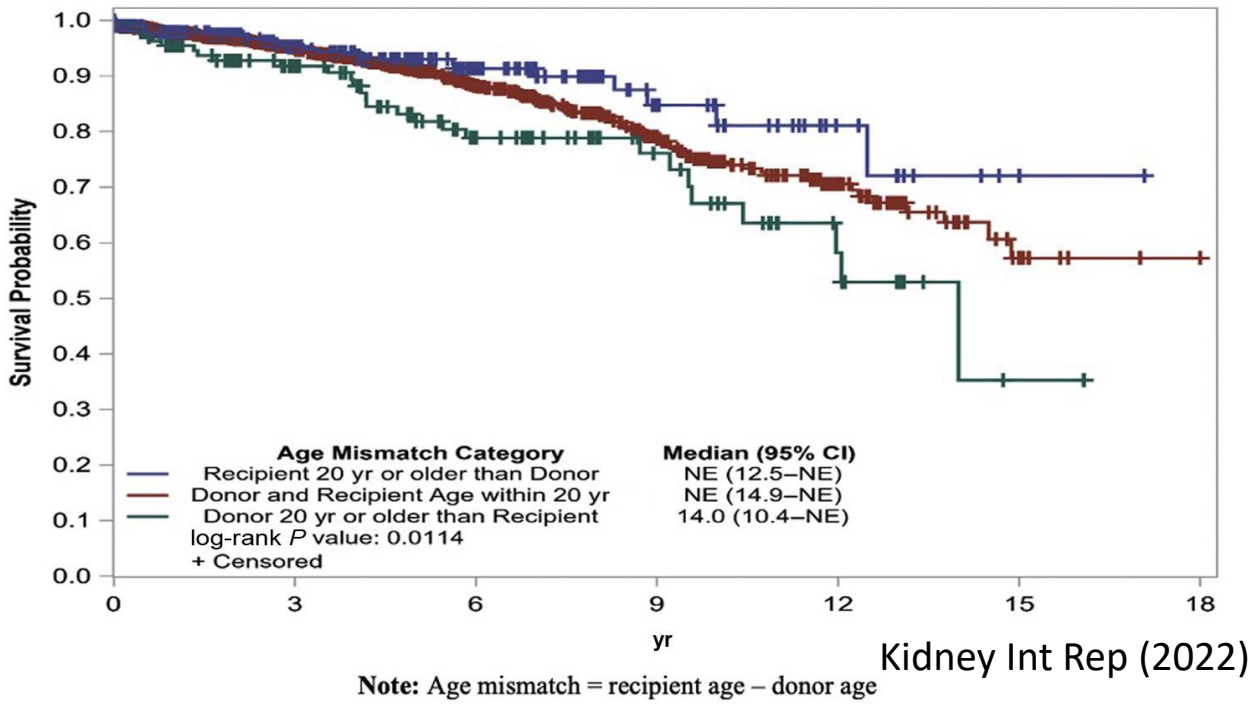
Georgina L. Irish [a,b,c], Lachlan C. McMichael [a,d], Matthew Kadatz [d,e], Neil Boudville Scott Campbell [h,i], Steven Chadban [j,k], Doris Chang [l], John Kanellis [m,n], Edward Sharples [o], John S. Gill [d,l,p,*], Philip A. Clayton [a,b,c]

SRTR	ANZDATA
N = 65 388	N = 4524

We conclude that the LKDPI does not discriminate DCGS and should not be used to promote CP participation in KPD programs.

Massie AB, et al. A Risk Index for Living Donor Kidney Transplantation. Am J Transplant. 2016.

Rethinking incompatibility in kidney transplantation, AJT 2021



Kidney Int Rep (2022)

478 hasta, DY ≥13 AY ise greft kaybı 9.5 kat fazla. *Kostakis ID, Clin Transplant. 2013*

100 bin hasta, Alıcı Kilo ≥30 Verici Kilo ; DSGF riski %22 daha fazla(<10 kg olanlara kıyasla) *Miller AJ,Clin J Am Soc Nephrol. 2017*

Rethinking incompatibility in kidney transplantation, AJT 2021

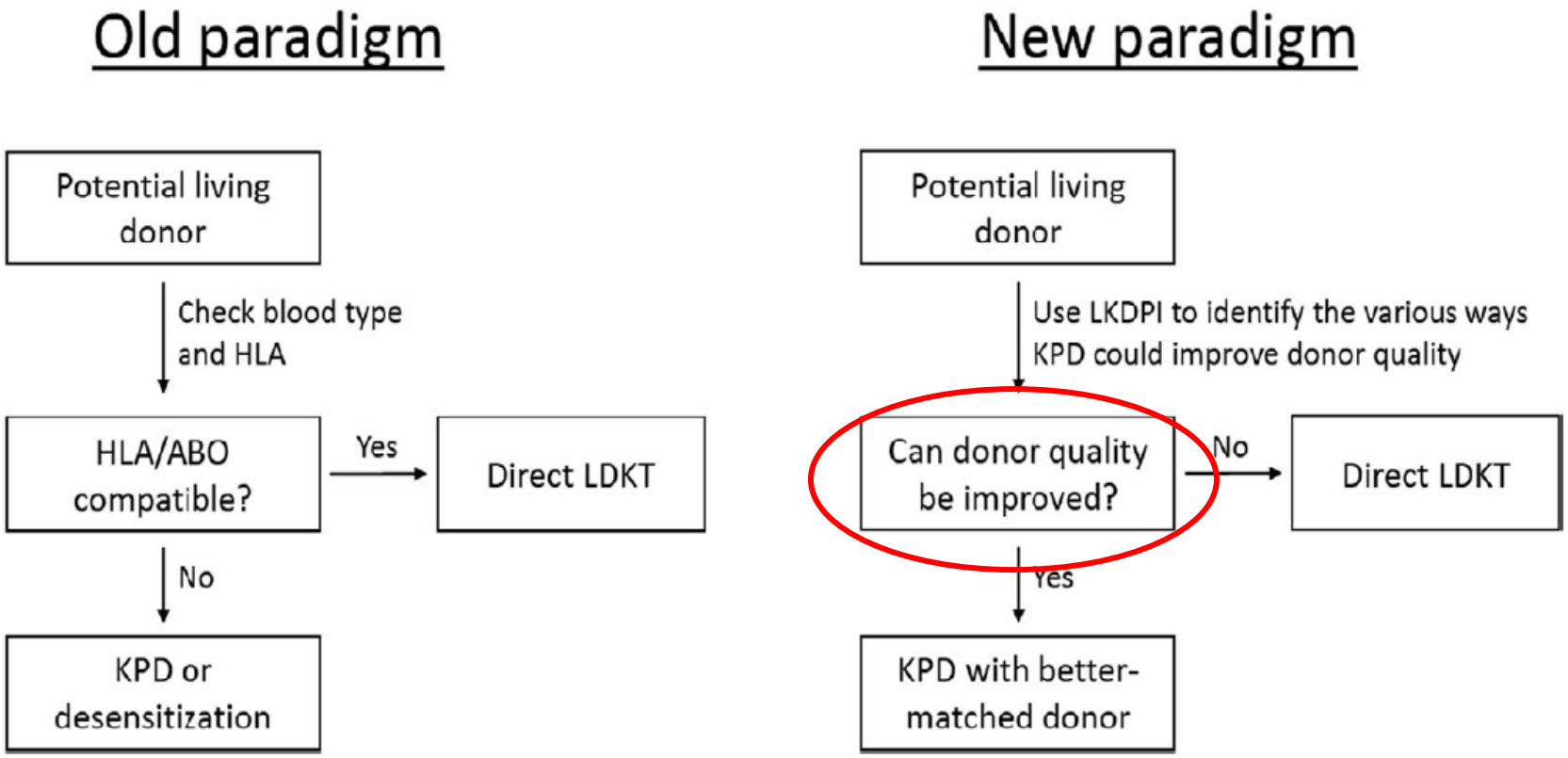
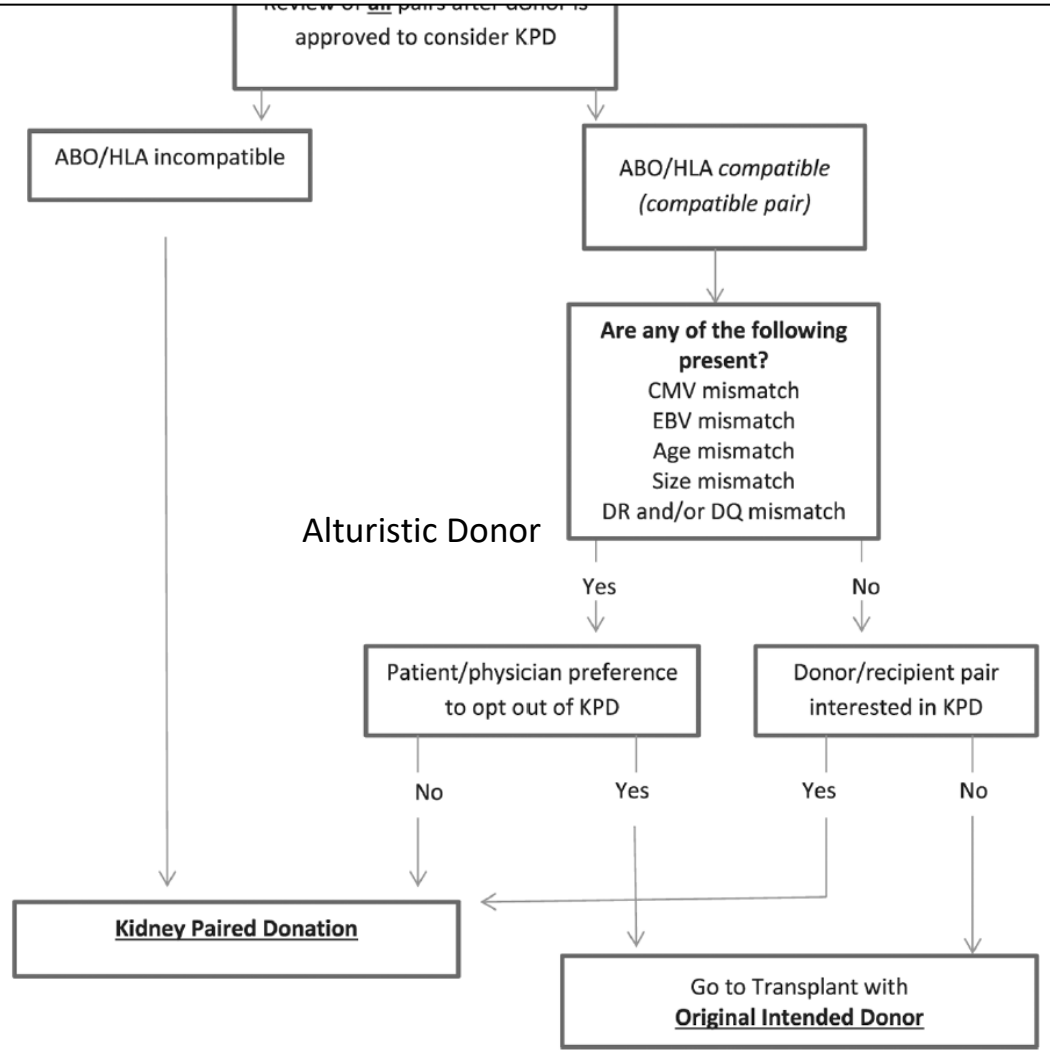
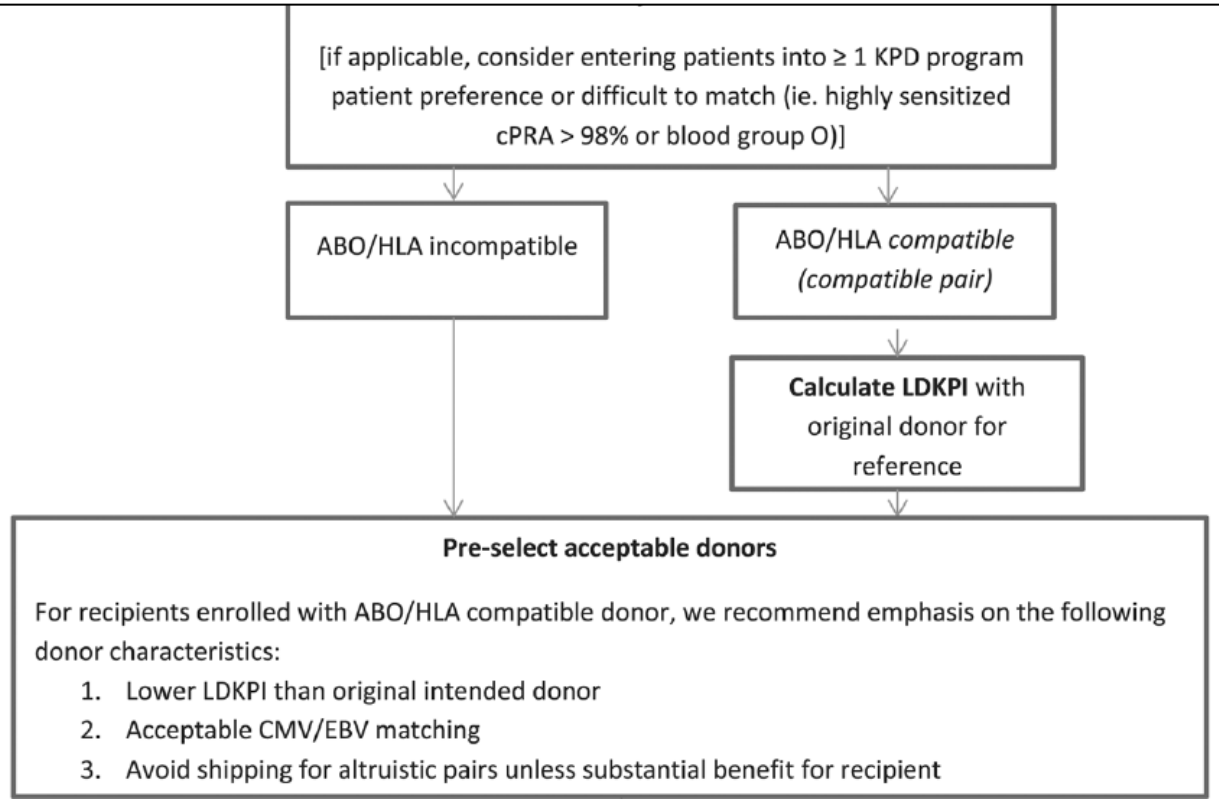


FIGURE 2 Paradigms of incompatibility. In the old paradigm of incompatibility, KPD was used primarily to avoid ABO/HLA-incompatibility, whereas ABO/HLA-compatible donors would undergo direct LDKT. Under the new paradigm of incompatibility, potential living donors are assessed for all types of incompatibilities using tools such as the LKDPI and other types of incompatibilities (such as viral

Ten Years of Kidney Paired Donation at Mayo Clinic: The Benefits of Incorporating ABO/HLA Compatible Pairs

İlk yıl canlı nakillerin %1.9 u, 10 yıl sonra %20.4 ü KPD havuzundan yapılmış.
54 tane uyumlu paylaşım yapılmış, yaş-boyut uyumsuzluğu nedeni ile gruba katılan alıcıların (28) yeni vericilerinin LKPDI indeksi ortalama 31.5(12.3,47, p<0.0001) puan azalmış.





332 TX, 9/2007-6/2018. (56 compatible, %44 preemptive)
Median time from KPD entry to transplantation was 89(42–187) day

Transplantation, 2020

Figure 3. Entry into Kidney Paired Donation Guideline.

Coopetition

13 languages

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From Wikipedia, the free encyclopedia

For the book, see Coopetition (book). For the 2000 FIRST Robotics Competition game, see Co-Opertition FIRST.

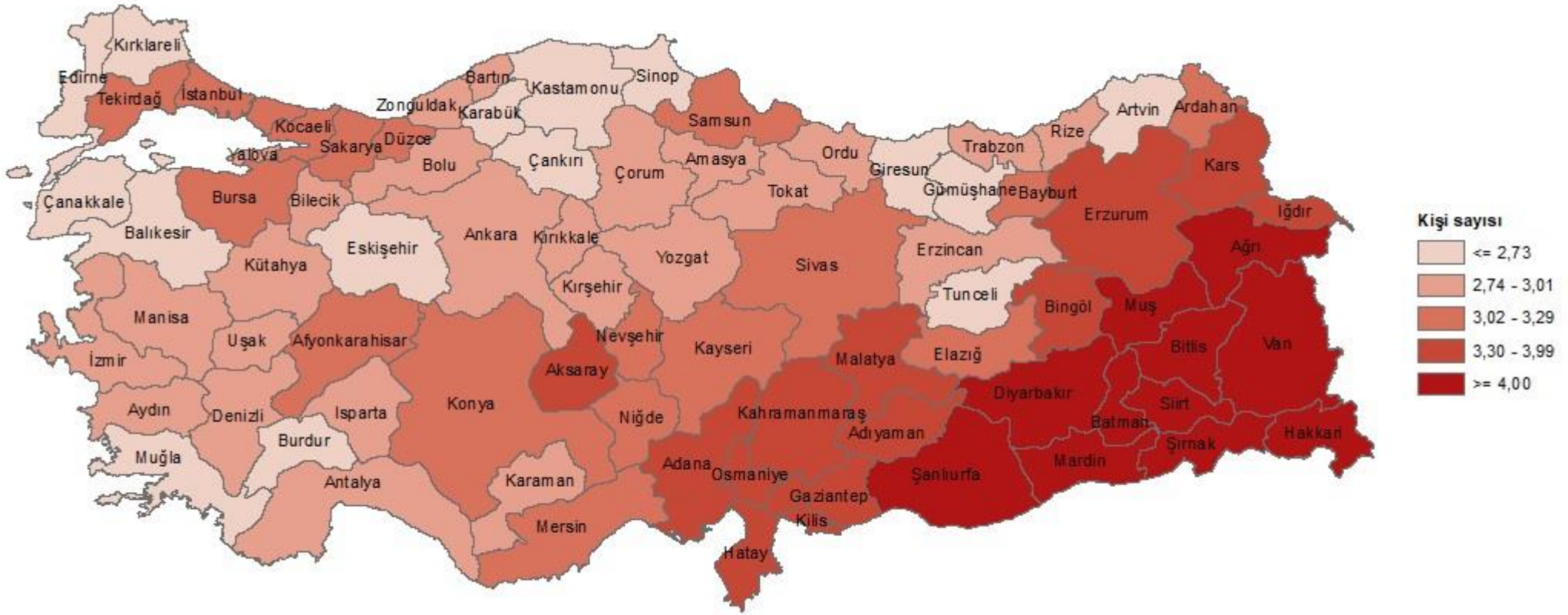
Coopetition or **co-opetition** (sometimes spelled **"coopertition"** or **"co-opertition"**) is a neologism coined to describe cooperative competition.

Desensitizasyon

Çapraz nakil

Desensitizasyon	Çapraz Nakil
Artmış immunsupresyon	Standart tedavi
enfeksiyon , malignite, erken dönem ölüm	
Artmış rejeksiyon riski	Azaltılabilir
Yüksek ilaç ve işlem maliyeti	
İşleme bağlı artmış kanama riski	
	Alıcı-verici psikolojisi
	Transfer riskleri
	Vazgeçme
	Soğuk iskemi

Ülkenin SOSYO-EKONOMİK koşulları	
Maliyet, ilaca ulaşma zorluğu	Çok sayıda akraba



Kaynak: TÜİK, Adrese Dayalı Nüfus Kayıt Sistemi, 2022