Kidney Paired Donation with HLA Desensitization – expanding the boundaries of sensitized patients

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ABSTRACT

The increasing incidence of chronic kidney disease along with the increasing rates of sensitized patients have led to an increasing, yet unmet, demand for kidney allografts. Several strategies have been employed to reduce this shortage, such as kidney paired donation, desensitization protocols and specific allocation systems for the highly sensitized. Despite the efforts, these patients remain on deceased and paired donation lists for extended periods of time, while some will never receive a kidney graft.
Advances in desensitization and immunosuppression must be used to strengthen already existing programs and favor "more compatible" matches to desensitize over non-existing compatible pairs.
We present a successful case of two kidney paired transplants with desensitization of both highly sensitized candidates.

Keywords: Kidney transplantation. HLA-incompatible transplantation. HLA-desensitization. Kidney paired donation.

Donación pareada de riñón con desensibilización por complejo principal de histocompatibilidad (HLA): ampliar los límites de los pacientes sensibilizados

La creciente incidencia de la enfermedad renal crónica junto con el aumento de las tasas de pacientes sensibilizados han llevado a una demanda continua, aunque no satisfecha, de aloinjertos de riñón. Se han empleado varias estrategias para reducir este déficit, como la donación pareada de riñón, los protocolos de desensibilización y los sistemas de asignación específicos para personas altamente sensibilizadas. A pesar de los esfuerzos, estos pacientes permanecen en las listas de donantes fallecidos y pareados durante largos periodos de tiempo, mientras que algunos nunca recibirán un trasplante de riñón.
Los avances en desensibilización e inmunosupresión deben utilizarse para fortalecer los programas ya existentes y favorecer las coincidencias «más compatibles» para desensibilizar frente a parejas compatibles inexistentes.
Presentamos un caso exitoso de dos trasplantes renales pareados con desensibilización de ambos candidatos altamente sensibilizados.

Palabras clave: *Trasplante renal. Trasplante incompatible con HLA. Desensibilización por HLA. Donación renal pareada.*

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INTRODUCTION

Kidney transplantation is the treatment of choice for end-stage chronic kidney disease (CKD), improving the quality and quantity of life for most patients when compared with maintenance dialysis[1,2].

The increasing incidence of CKD and the resulting shortage of donor kidneys led to the introduction of several strategies to expand deceased kidney donation, such as expanded criteria for deceased donors[3,4] and donation after circulatory death[5-7]. However, this modality is ever limited by the number of deceased donors.

Living kidney donation –the best modality when compared with equally-matched deceased donation– offers longer patient and graft survival rates[8,9], but has been hindered by an increasingly sensitized population in such a way that threatens kidney donation itself, as the grafts cannot be offered to their pairs. Beyond pregnancies and blood transfusions, the increasing number of dialysis patients with previous allografts has been adding to this problem. These potential recipients have thus been relegated to the ever-expanding deceased-donor waiting list. To overcome this immunological barrier and further expand living kidney transplantation, the concept of paired donation was introduced[10-15] and desensitization protocols have emerged to allow transplantation of previously incompatible grafts[16,17]. Another strategy lies in the implementation of specific allocation programs for the highly sensitized (HS), such as the Spanish *Plan Nacional de Acceso al Trasplante a Pacientes Hiperinmunizados* (PATHI) and the North American *Kidney Allocation System* (KAS)[18-20].

These strategies must be viewed as complementary, so that sensitized patients are offered the best chances of receiving a kidney transplant.

CASE REPORT

Pair 1: A 67-year-old female with autosomal dominant polycystic kidney disease on hemodialysis was a candidate for a first kidney transplant from her son-in-law. Known sensitizing events were limited to 1 pregnancy. ABO Rh typing was O+ and the calculated panel of reactive antibodies (cPRA) considering human leukocyte antigen-ABCDRB1 (HLA) and the Eurotransplant reference population[21] was 91.1%. She presented an anti-HLA-B35 donor-specific antibody (DSA) with mean fluorescence intensity (MFI) of 13231 against her potential donor, a 44-year-old male, also O+. Complement-dependent cytotoxicity crossmatch (CDC-XM) was negative, but flow cytometry crossmatch (FC-XM) was positive for B and T-cells. The pair was enrolled in the Portuguese kidney exchange program (KEP).

Pair 2: A 43-year-old female with primary membranous nephropathy received a pre-emptive kidney allograft from her mother at the age of 21. She had 2 non-biopsy proven rejection episodes treated with methylprednisolone. After 9 years, a biopsy was performed for graft dysfunction and proteinuria, revealing membranous nephropathy recurrence. Slow, progressive dysfunction ensued under renin-angiotensin-aldosterone blockade, and the patient started peritoneal dialysis 20 years after transplantation. There were no additional sensitizing events nor immunologic or infectious complications recorded. ABO Rh typing was O+, cPRA 90.2%, with anti-HLA Cw antibodies against all Cw antigens except her own Cw7.

The patient presented with a C1q-binding anti-HLA-Cw5 DSA with MFI 18536 against her potential donor, who shared the same blood type. CDC-XM was negative, but FC-XM was positive for both B and T-cells. The pair was enrolled in the Portuguese KEP.

Crossmatch between candidate from pair 1 (R1) and potential donor from pair 2 (D2) was remarkable for an anti-HLA-B44 DSA with MFI 5514, negative CDC-XM, positive FC-XM for T-cells with a median channel shift (MCS) of 150 (positive >50) and negative FC-XM for B-cells.

Crossmatch between candidate from pair 2 (R2) and potential donor from pair 1 (D1) was remarkable for an anti-HLA-Cw4 DSA with MFI 8669, negative CDC-XM, positive FC-XM for T-cells with a MCS of 242 (positive >50) and negative FC-XM for B-cells.

Given the better immunological profile of the paired crossmatch, both candidates underwent desensitization as per each hospital's protocol with plasmapheresis, rituximab, and high dose 2 g/kg IV immunoglobulin. The repeat crossmatch of R1-D2 after desensitization revealed a substantially reduced MFI count of 2203 for the anti-HLA-B44 DSA, with a FC-XM MCS of 133 for T-cells and 52 for B-cells (FC-XM for B-cells was a false negative).

Repeat crossmatch of R2-D1 revealed a decreased MFI of 5659 for the anti-HLA-Cw4 DSA (the FC-XM MCS was not performed at this point).

We decided to proceed with the paired transplantation. Candidates underwent induction immunosuppressive therapy with antithymocyte globulin, methylprednisolone, tacrolimus, and mycophenolate mofetil, with successfully paired transplantation and immediate function of both grafts.

Maintenance immunosuppressive therapy was the same for both receptors, comprising tacrolimus, mycophenolate mofetil and prednisolone.

At hospital discharge, R1 had a serum creatinine (Cr) of 0.59 mg/dL and R2 had Cr 0.9 mg/dL, both with bland urinalysis.

Infectious complications of R1 included a successfully treated pulmonary aspergillosis 1 year after transplantation and a BK *polyomavirus* viremia treated with suspension of the antimetabolite. R1 also had a curative nephrectomy for a localized renal cell carcinoma of the left native kidney, 5 years post transplantation. Everolimus was not tolerated due to gastrointestinal symptoms, so the patient maintained low-dose tacrolimus whilst keeping the antimetabolite suspended.

R2 has had no evidence of oncologic diseases. Infectious complications involved a successfully treated acute pyelonephritis and a BK *polyomavirus* viremia resolved with conversion from tacrolimus to everolimus.

After 6 years of follow-up, both receptors have functional grafts: R1 has Cr 0.67 mg/dL, CKD-EPI estimated glomerular filtration rate (eGFR) of 92 mL/min/1.73 m^2 [22], and no proteinuria; R2 has Cr 1.09 mg/dL, CKD-EPI eGFR of 65 mL/min/1.73 m^2, and no proteinuria. Both receptors have had no evidence of antibody-mediated rejection or other immunologic complications. There have been not *de novo* DSAs nor increasing MFI for the preformed ones.

DISCUSSION

The definition of "highly sensitized" is unclear, as the PRA cut-off value and its method of calculation vary among different countries. Generally, this term is applied to candidates with a cPRA >80%[23,24], but the Spanish PATHI considers cPRA values >98%[18] and Portugal mostly relies on cytotoxic assays, with cut-off values of CDC-PRA >50-80%[25]. Despite the method, we have a very high percentage of HS patients, with 25.7% of the wait-listed presenting with a cPRA ≥98%[26]. This high allosensitization rate –explained in part by the 2007 allocation system that overly awards "time on dialysis" points over "HLA compatible" points– along with an O blood type imbalance, result in lower transplantability among these patients, even within the KEP[27-29]. A paired exchange program's potency depends critically on the size of the match pool[30] and, in this regard, there is an unmet need to widen the size of our national KEP. More pairs must enroll in these programs to improve matching, and the inclusion of HLA mismatched compatible pairs has shown to be a promising strategy, not only by enabling transplantation of HLA-incompatible (HLAi) pairs, but also by providing better-matched allografts for the compatible ones[29,31-33]. Beyond ABO and HLA matching, compatibility extends to age, gender, size and viral status (of *Cytomegalovirus* and *Epstein-Barr* virus), as they also impact patient and graft survival[34-38]. As such, better matching of these factors may bring additional benefits for the ABO and HLA-compatible (HLAc) pairs enrolled in the paired donation programs. Portuguese legislation has only recently encompassed the inclusion of such HLAc pairs in the exchange program, which may prove to be a step towards increasing the strength of our KEP. Additionally, our center's inclusion in the international *South Alliance for Transplants* program in 2018 has already granted international kidney paired exchanges and is certain to represent an important reinforcement strategy for a country that lacks a national program for the HS. These programs for the "hypersensitized" have undoubtedly been successful, with Spain reporting an impressive 30% of PATHI patients transplanted from 2015 to 2019[18,39] and the US reporting a decrease in the transplant waiting time from 19 to 3,2 years in candidates with a cPRA 98-100%[40].

Despite HLA-compatibility being associated with better outcomes than HLAi transplantation[17,41-42], a survival benefit from transplanting HLA desensitized patients has been reported over remaining on the transplant waiting list on maintenance dialysis[30,43-44]. By contrast, UK data from Manook et al. opposed that of North American reports, stating that desensitization has no detrimental effect on patient survival but doesn't offer a survival benefit over remaining on the UK kidney transplant waiting list.[45] Be that as it may, desensitization therapies are not risk-free, but can be the only option for well-studied and selected patients. Prospective studies to identify such populations are lacking, as are randomized controlled trials comparing existing desensitization protocols. In fact, not only do PRA cut-off values lack standardization, but the definitions of successful desensitization - namely the need to have both CDC and FC negative crossmatch versus only CDC negative crossmatch, and the cut-off MFI counts – vary among different centers.[39] In our report, the decision to proceed with the paired exchange had to be thoroughly addressed, since the candidates presented with a post-desensitization positive FC crossmatch with significant MFI >1000, which would render them non-desensitized and effectively untransplantable according to some centers' criteria[39]. Ultimately, the risks and benefits of incompatible living donor transplantation must be weighed against waiting for compatible deceased or paired donation, emphasizing that, in most studies, transplantation provides a survival benefit and improved quality of life[43,44] and that longer pre-transplant dialysis is associated with poorer outcomes following transplantation[46,47].

Despite the lack of randomized controlled trials comparing desensitization protocols, its effectiveness is clear and should be perceived as part of a kidney exchange program to allow transplantation of the HS for whom a compatible donor might not be available, in favor of a "more compatible" match to desensitize[30,48]. Since these therapies may not bring additional benefits to some populations[45], we need a careful and individualized selection of a very comorbid population, often on dialysis for a long time. This highlights the vital need for additional studies to identify patients that will benefit the most from desensitization strategies and those that would not.

We report a case of two O blood type, HLA sensitized candidates with very high antibody titers against their potential donors' "unacceptable antigens"[49]. Given the scarce probabilities of receiving a kidney graft from the deceased-donor list, these patients' realistic chances of being transplanted laid on a kidney paired donation. The paired crossmatch exhibited a lower immunologic risk profile, albeit still under considerable risk that did not preclude desensitization, as DSAs with high MFI counts were present for both candidates[50]. However, since desensitizing these kidney exchange pairs may have represented the single transplantation opportunity for these patients, we decided to proceed with the paired exchange, which has proven to be a successful long-term strategy. Indeed, after 6 years, both receptors retain good graft function, no proteinuria, and no immunologic complications. Moreover, the risk of renal cell carcinomas in end-stage CKD and kidney transplant recipients is up to 15-fold increased, such that we cannot definitively relate the complication exhibited by R1 with the immunosuppression[51].

CONCLUSION

No patient should be labeled "untransplantable" based on ABO and HLA incompatibility but be provided with individualized and realistic counseling regarding their expectable waiting times, so that informed, rational approaches –like paired exchange with desensitization– can be made. While newer and promising desensitization drugs arrive[52], the "basics" of transplantation must not be neglected. The authors acknowledge the urgent need to review the Portuguese allocation system, create specific programs for allocation of the HS –like the Spanish PATHI– and strengthen the already existing exchange programs with desensitization protocols.

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Conflicts of interest

The authors have no conflicts of interest to declare.

REFERENCES

1. Schnuelle P, Lorenz D, Trede M, Van Der Woude FJ. Impact of renal cadaveric transplantation on survival in end-stage renal failure: evidence for reduced mortality risk compared with hemodialysis during long-term follow-up. Journal of the American Society of Nephrology. JASN. 1988;9: 2135-41. https://doi.org/10.1681/ASN.V9112135.
2. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. The New England journal of medicine, 1999;341(23), 1725–1730. https://doi.org/10.1056/NEJM199912023412303.
3. Kling CE, Perkins JD, Johnson CK, Blosser CD, Leca N, Sibulesky L. Utilization of Standard Criteria Donor and Expanded Criteria Donor Kidneys After Kidney Allocation System Implementation. Ann Transplant. 2018;23:691-703. https://doi.org/10.12659/AOT.910504.
4. Stallone G, Grandaliano G. To discard or not to discard: transplantation and the art of scoring. Clin Kidney J. 2019;12:564-8. https://doi.org/10.1093/ckj/sfz032.
5. Manyalich M, Nelson H, Delmonico FL. The need and opportunity for donation after circulatory death worldwide. Curr Opin Organ Transplant. 2018;23:136-41. https://doi.org/10.1097/MOT.0000000000000486.
6. O'Connor KJ, Delmonico FL. Increasing the supply of kidneys for transplantation. Semin Dial. 2005;18:460-2. https://doi.org/10.1111/j.1525-139X.2005.00089.x.
7. Barnieh L, Collister D, Manns B, Lam NN, Shojai S, Lorenzetti D, et al. A Scoping Review for Strategies to Increase Living Kidney Donation. Clin J Am Soc Nephrol. 2017;12:1518-27. https://doi.org/10.2215/CJN.01470217.
8. Merion RM, Ashby VB, Wolfe RA, Distant DA, Hulbert-Shearon TE, Metzger RA, et al. Deceased-donor characteristics and the survival benefit of kidney transplantation. JAMA. 2005;294:2726-33. https://doi.org/10.1001/jama.294.21.2726.
9. Sánchez-Escuredo A, Alsina A, Diekmann F, Revuelta I, Esforzado N, Ricart MJ, et al. Economic analysis of the treatment of end-stage renal disease treatment: living-donor kidney transplantation versus hemodialysis. Transplant Proc. 2015;47:30-3. https://doi.org/10.1016/j.transproceed.2014.12.005.
10. Rapaport FT. The case for a living emotionally related international kidney donor exchange registry. Transplant Proc. 1986;18 (Suppl. 2):5-9.
11. de Klerk M, Zuidema WC, Ijzermans JN, Weimar W. Strategies to expand the living donor pool for kidney transplantation. Front Biosci. 2008;13:3373-80. https://doi.org/10.2741/2932.
12. Ferrari P, Woodroffe C, Christiansen FT. Paired kidney donations to expand the living donor pool: the Western Australian experience. Med J Aust. 2009;190:700-3. https://doi.org/10.5694/j.1326-5377.2009.tb02642.x.
13. Glorie K, Haase-Kromwijk B, van de Klundert J, Wagelmans A, Weimar W. Allocation and matching in kidney exchange programs. Transpl Int. 2014;27:333-43. https://doi.org/10.1111/tri.12202.
14. Kute VB, Patel HV, Shah PR, Modi PR, Shah VR, Rizvi SJ, et al. Seventy-seven kidney paired donation transplantations at a single transplant centre in India led to an increase in living donor kidney transplantations in 2015. Clin Kidney J. 2017;10:709-14. https://doi.org/10.1093/ckj/sfx032.
15. Sethi S, Choi J, Toyoda M, Vo A, Peng A, Jordan SC. Desensitization: Overcoming the Immunologic Barriers to Transplantation. J Immunol Res. 2017;2017:6804678. https://doi.org/10.1155/2017/6804678.
16. Orandi BJ, Garonzik-Wang JM, Massie AB, Zachary AA, Montgomery JR, Van Arendonk KJ, et al. Quantifying the risk of incompatible kidney transplantation: a multicenter study. Am J Transplant. 2014;14:1573-80. https://doi.org/10.1111/ajt.12786.
17. Fernández C, Calvo M, Leite N, López A, Ferreiro T, Ribera R, et al. Kidney transplantation from HLA-incompatible live donors: Efficiency and outcome of 32 patients after desensitisation. Trasplante renal procedente de donante vivo HLA incompatible: Eficacia y pronóstico en 32 pacientes tras desensibilización. Nefrologia. 2017;37:638-45. https://doi.org/10.1016/j.nefro.2017.06.006.
18. Tambur AR, Campbell P, Chong AS, Feng S, Ford ML, Gebel H, et al. Sensitization in transplantation: Assessment of risk (STAR) 2019 Working Group Meeting Report. Am J Transplant. 2020;20:2652-68. https://doi.org/10.1111/ajt.15937.
19. Formica RN, Jr. A critical assessment on kidney allocation systems. Transplant Rev. 201731:61-7. https://doi.org/10.1016/j.trre.2016.10.002.
20. Eurotransplant virtual PRA calculator reference. https://www.etrl.org/vPRA.aspx.
21. Delgado C, Baweja M, Burrows NR, Crews DC, Eneanya ND, Gadegbeku CA, et al. Reassessing the Inclusion of Race in Diagnosing Kidney Diseases: An Interim Report From the NKF-ASN Task Force. J Am Soc Nephrol. 2021;32:1305-17. https://doi.org/10.1053/j.ajkd.2021.03.008.
22. Sethi S, Najjar R, Peng A, Mirocha J, Vo A, Bunnapradist S, et al. Allocation of the Highest Quality Kidneys and Transplant Outcomes Under the New Kidney Allocation System. Am J Kidney Dis. 2019;73:605-614. https://doi.org/10.1053/j.ajkd.2018.12.036.

23. Cecka JM. Calculated PRA (CPRA): the new measure of sensitization for transplant candidates. Am J Transplant. 2010;10:26-9. https://doi.org/10.1111/j.1600-6143.2009.02927.x.
24. Magriço R, Malheiro J, Tafulo S, Pedroso S, Almeida M, Martins L, et al. Implications for patients waiting for a kidney transplant of using the calculated panel reactive antibody (cPRA). Port J Nephrol Hypert. 2010;30:185-93.
25. Blood and Transplantation Center of Porto. Instituto Português do Sangue e da Transplantação. Unpublished results from March 2022.
26. Glander P, Budde K, Schmidt D, Fuller TF, Giessing M, Neumayer HH, et al. The 'blood group O problem' in kidney transplantation--time to change? Nephrol Dial Transplant. 2010;25:1998-2004. https://doi.org/10.1093/ndt/gfp779.
27. Tafulo S, Malheiro J, Dias L, Mendes C, Osório E, Martins LS, et al. Low transplantability of 0 blood group and highly sensitized candidates in the Portuguese kidney allocation algorithm: quantifying an old problem in search of new solutions. HLA. 2010;88:232-8. https://doi.org/10.1111/tan.12895.
28. Tafulo S, Malheiro J, Dias L, Lobato L, Ramalhete L, Martinho A, et al. Improving HLA matching in living donor kidney transplantation using kidney paired exchange program. Transpl Immunol. 2020;62:101317. https://doi.org/10.1016/j.trim.2020.101317.
29. Holscher CM, Jackson KR, Segev DL. Transplanting the Untransplantable. Am J Kidney Dis. 2020;75:114-23. https://doi.org/10.1053/j.ajkd.2019.04.025.
30. Basu A, Prieto M, Kosberg C, Mai ML, Khamash HA, Jadlowiec CC, et al. Ten Years of Kidney Paired Donation at Mayo Clinic: The Benefits of Incorporating ABO/HLA Compatible Pairs. Transplantation. 2020;104:1229-38. https://doi.org/10.1097/TP.0000000000002947.
31. Gill JS, Tinckam K, Fortin MC, Rose C, Shick-Makaroff K, Young K, et al. Reciprocity to Increase Participation of Compatible Living Donor and Recipient Pairs in Kidney Paired Donation. Am J Transplant. 2017;17:1723-1728. https://doi.org/10.1111/ajt.14275.
32. Ferrari P, Cantwell L, Ta J, Woodroffe C, D'Orsogna L, Holdsworth R. Providing Better-Matched Donors for HLA Mismatched Compatible Pairs Through Kidney Paired Donation. Transplantation. 2017.101:642-8. https://doi.org/10.1097/TP.0000000000001196.
33. Kostakis ID, Moris DN, Barlas A, Bokos I, Darema M, Theodoropoulou E, et al. Impact of donor and recipient age difference on long-term allograft survival after living donor renal transplantation: analysis of 478 cases. Clin Transplant. 2013;27:838-43. https://doi.org/10.1111/ctr.12219.
34. Miller AJ, Kiberd BA, Alwayn IP, Odutayo A, Tennankore KK. Donor-Recipient Weight and Sex Mismatch and the Risk of Graft Loss in Renal Transplantation. Clin J Am Soc Nephrol. 2017;12:669-76. https://doi.org/10.2215/CJN.07660716.
35. McGee J, Magnus JH, Islam TM, Jaffe BM, Zhang R, Florman SS, et al. Donor-recipient gender and size mismatch affects graft success after kidney transplantation. J Am Coll Surg. 2010;210:718-725. e1. https://doi.org/10.1016/j.jamcollsurg.2009.12.032.
36. Sampaio MS, Cho YW, Shah T, Bunnapradist S, Hutchinson IV. Impact of Epstein-Barr virus donor and recipient serostatus on the incidence of post-transplant lymphoproliferative disorder in kidney transplant recipients. Nephrol Dial Transplant. 2012;27:2971-9. https://doi.org/10.1093/ndt/gfr769.
37. Leeaphorn N, Garg N, Thamcharoen N, Khankin EV, Cardarelli F, Pavlakis M. Cytomegalovirus mismatch still negatively affects patient and graft survival in the era of routine prophylactic and preemptive therapy: A paired kidney analysis. Am J Transplant. 2019;19:573-84. https://doi.org/10.1111/ajt.15183.
38. Fernández Rivera C, Calvo Rodríguez M, Ferreiro Hermida T, Astudillo Jarrín D, Rodríguez Magariños C, López Muñiz A, et al. Trasplante renal con antígenos leucocitarios humanos (HLA) incompatibles. Revisión. Nefrología (English Edition). 2021;13:10-29.
39. Formica RN Jr, Kulkarni S. Being Thoughtful about Desensitization. Clin J Am Soc Nephrol. 2017;12:1878-80. https://doi.org/10.2215/CJN.09000817.
40. Amrouche L, Aubert O, Suberbielle C, Rabant M, Van Huyen JD, Martinez F, et al. Long-term Outcomes of Kidney Transplantation in Patients with High Levels of Preformed DSA: The Necker High-Risk Transplant Program. Transplantation. 2017;101:2440-8. https://doi.org/10.1097/TP.0000000000001650.
41. Orandi BJ, Luo X, King EA, Garonzik-Wang JM, Bae S, Montgomery RA, et al. Hospital readmissions following HLA-incompatible live donor kidney transplantation: A multi-center study. Am J Transplant. 2018;18:650-8. https://doi.org/10.1111/ajt.14472.
42. Montgomery RA, Lonze BE, King KE, Kraus ES, Kucirka LM, Locke JE, et al. Desensitization in HLA-incompatible kidney recipients and survival. N Engl J Med. 2011;365:318-26. https://doi.org/10.1056/NEJMoa1012376.
43. Orandi BJ, Luo X, Massie AB, Garonzik-Wang JM, Lonze BE, Ahmed R, et al. Survival Benefit with Kidney Transplants from HLA-Incompatible Live Donors. N Engl J Med. 2016;374:940-50. https://doi.org/10.1056/NEJMoa1508380.
44. Manook M, Koeser L, Ahmed Z, Robb M, Johnson R, Shaw O, et al. Post-listing survival for highly sensitised patients on the UK kidney transplant waiting list: a matched cohort analysis. Lancet. 2017;389:727-34. https://doi.org/10.1016/S0140-6736(16)31595-1.
45. Meier-Kriesche HU, Schold JD. The impact of pretransplant dialysis on outcomes in renal transplantation. Semin Dial. 2005;18:499-504. https://doi.org/10.1111/j.1525-139X.2005.00096.x.
46. Aufhauser DD Jr, Peng AW, Murken DR, Concors SJ, Abt PL, Sawinski D, et al. Impact of prolonged dialysis prior to renal transplantation. Clin Transplant. 2018;32:e13260. https://doi.org/10.1111/ctr.13260.
47. Montgomery RA. Renal transplantation across HLA and ABO antibody barriers: integrating paired donation into desensitization protocols. Am J Transplant. 2010;10:449-57. https://doi.org/10.1111/j.1600-6143.2009.03001.x.
48. Gloor JM, Winters JL, Cornell LD, Fix LA, DeGoey SR, Knauer RM, et al. Baseline donor-specific antibody levels and outcomes in positive crossmatch kidney transplantation. Am J Transplant. 2010;10:582-9. https://doi.org/10.1111/j.1600-6143.2009.02985.x.
49. Malheiro J, Tafulo S, Dias L, Martins S, Fonseca I, Beirão I, et al. Impact on mid-term kidney graft outcomes of pretransplant anti-HLA antibodies detected by solid-phase assays: Do donor-specific antibodies tell the whole story? Hum Immunol. 2017;78:526-33. https://doi.org/10.1016/j.humimm.2017.07.011.
50. Goujon A, Verhoest G, Sallusto F, Branchereau J, Boutin JM, Bessede T, et al. Renal cell carcinoma in candidates for renal transplantation and recipients of a kidney transplant: The French guidelines from CTAFU. Prog Urol. 2021;31:18-23. https://doi.org/10.1016/j.purol.2020.04.030
51. Jordan SC, Legendre C, Desai NM, Lorant T, Bengtsson M, Lonze BE, et al. Imlifidase Desensitization in Crossmatch-positive, Highly Sensitized Kidney Transplant Recipients: Results of an International Phase 2 Trial (Highdes). Transplantation. 2021;105:1808-1817. https://doi.org/10.1097/TP.0000000000003496.