SUPERIOR SURVIVAL OUTCOMES IN ABO-INCOMPATIBLE KIDNEY TRANSPLANT VS. KIDNEY-PAIRED DONATION: A SINGLE-CENTER COMPARATIVE COHORT STUDY

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Conflict of interests

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Justification
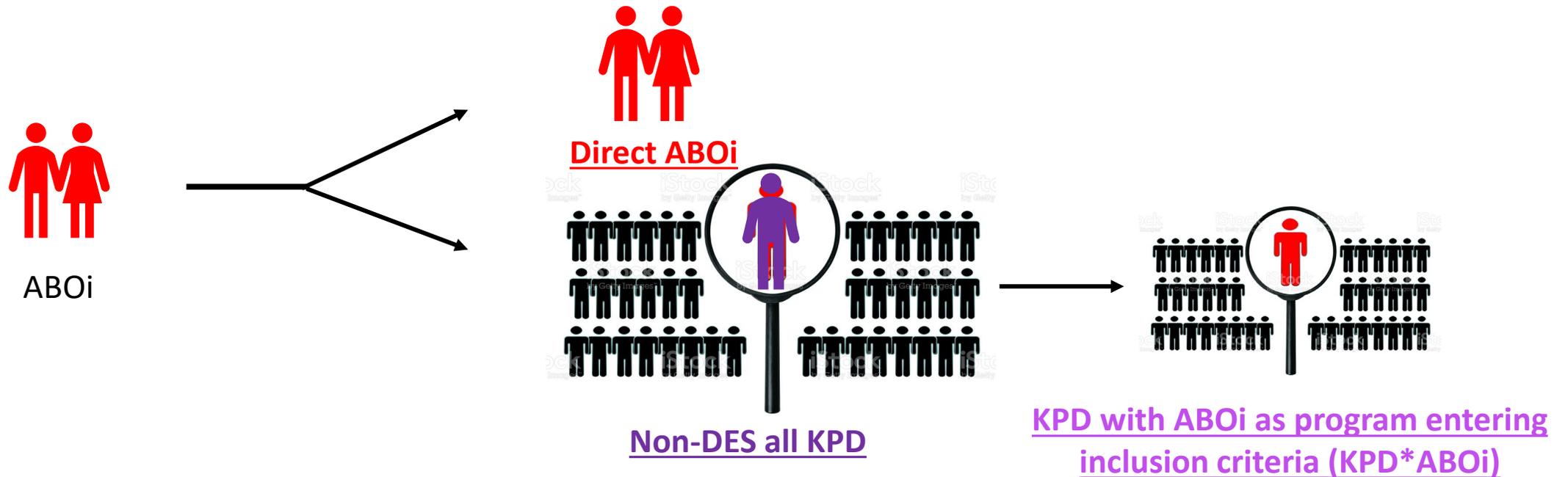
- Worse patient and death-censored graft survival have been shown in ABOi LDKT than ABOc, but not for all observation period time and blood group incompatibilities[1-3]

- KPD offers comparable results with ABOc, with some rates better that already reported in ABOi[4]

- However, sometimes we need to find a suitable donor in **a real scenario**, comparing the options we have, and the potential direct ABOi LDKT could be the best option in terms of patient´s survival[5], but ABOi and crossing processes handled by the transplant centers are different[6,]

- In addition, limitations are also coming from different group of ages for the balance of the potential effect of DES or the impact of the waiting time[7-9]

- Thus, rethinking incompatibility is neccesary[10]

[1]*Scort FG et al, Lancet 2019;* [2]*Weeerd and Betjes, CJASN 2018;* [3]*Lonze et al, Transplant Int 2017;* [4]*Leeser et al, CJASN 2020;* [5]*Massie et al, AJKD Nov 2020;* [6]*Manook et al, Transplant Int 2021;* [7]*Kim et al, Transplant Int 2021;* [8]*Hattori et al, Transplantation 2018;* [9]*Yee Hew et al, Pediatric Transplantation 2022;* [10]*Personal viewpoint of Jackson and Segev, Am J Transplant 2022*

Hypothesis and objective

ABOi LDKT offers acceptable long-term results, with higher short-term mortality and antibody mediated rejection comparing with ABOc LDKT. But, comparing with **the most suitable comparable chances**, KPD or DDKT, such differences disappear

Our objective is to evaluate the direct ABOi LDKT against the all none-DES KPD, and specifically with the KPD with ABOi as program entering inclusion criteria (KPD*ABOi)

ABOi

Direct ABOi

Non-DES all KPD

KPD with ABOi as program entering inclusion criteria (KPD*ABOi)

Material and methods
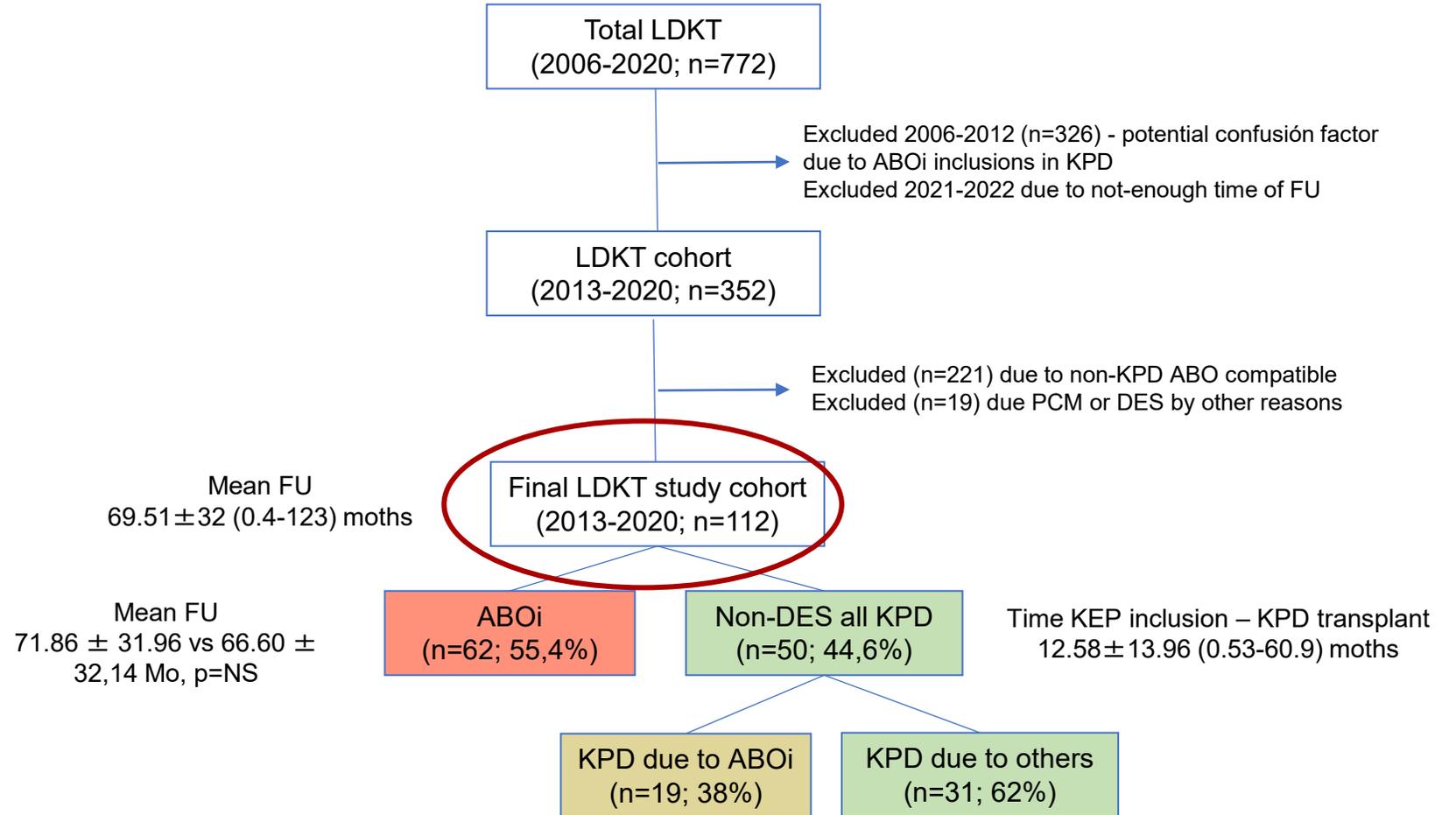
Retrospective, unicenter study

Selected sample sizes and adjusted by objectives control group

ABOi DES therapy according initial isoagglutinin titers; mainly based on RTX, PE vs eIDAS, and single-dose IGIV

National Spanish KEP based on prohibited antigens and BG compatibility (possibility of ABOi and DES in KEP)

Statistical analysis

Ethical comitte approval

Total LDKT
(2006-2020; n=772)

Excluded 2006-2012 (n=326) - potential confusión factor due to ABOi inclusions in KPD
Excluded 2021-2022 due to not-enough time of FU

LDKT cohort
(2013-2020; n=352)

Excluded (n=221) due to non-KPD ABO compatible
Excluded (n=19) due PCM or DES by other reasons

Mean FU
69.51±32 (0.4-123) moths

Final LDKT study cohort
(2013-2020; n=112)

Mean FU
71.86 ± 31.96 vs 66.60 ± 32,14 Mo, p=NS

ABOi
(n=62; 55,4%)

Non-DES all KPD
(n=50; 44,6%)

Time KEP inclusion – KPD transplant
12.58±13.96 (0.53-60.9) moths

KPD due to ABOi
(n=19; 38%)

KPD due to others
(n=31; 62%)

Results I. Patient survival in the final LDKT study cohort (2013-2020; n=112)

Survival estimation 348,7 months (Std error: 24,8) (300,1-397,3 95%CI)

Results I. Patient survival in the final LDKT study cohort (2013-2020; n=112)

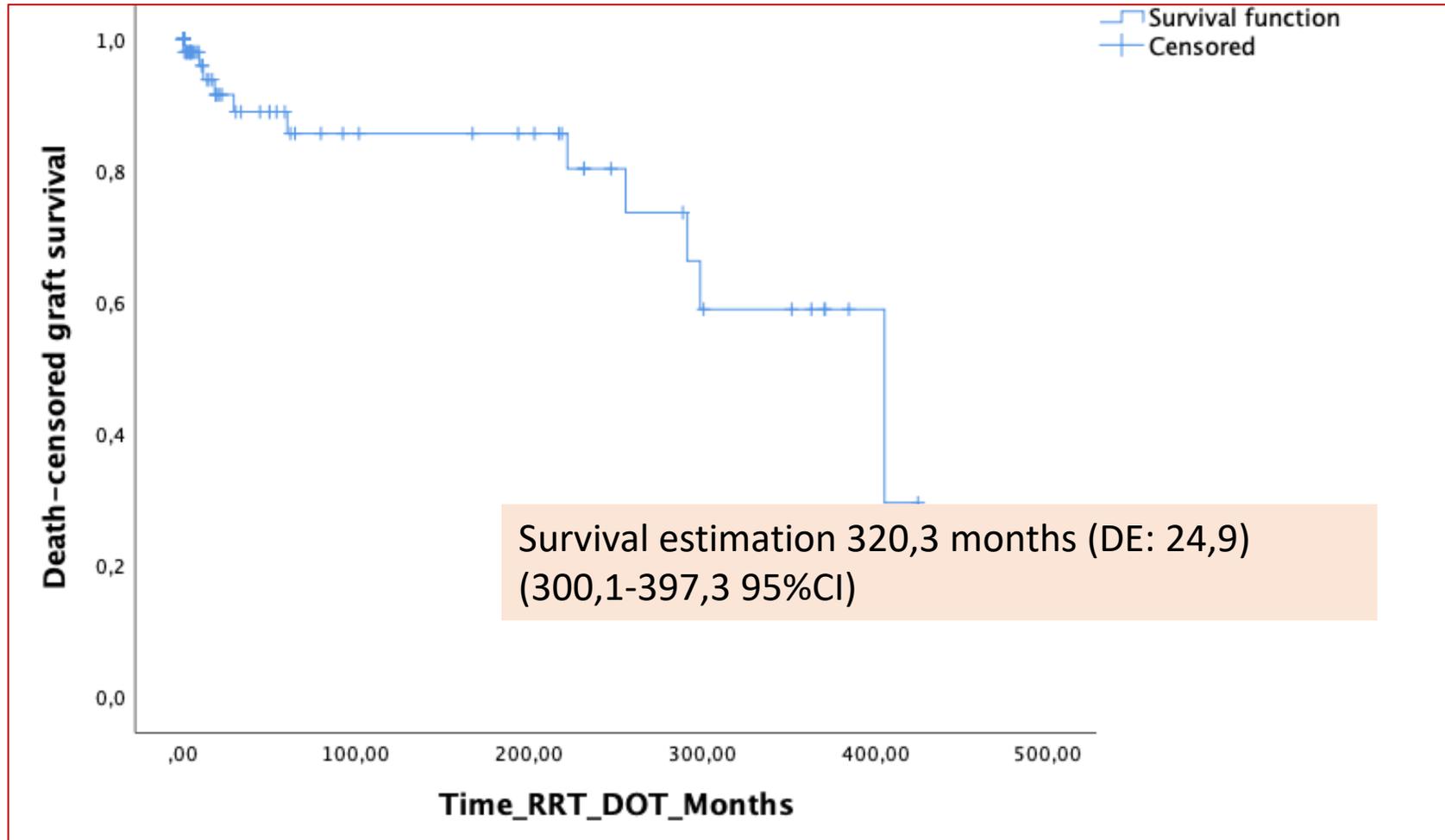|	Survival (n=102)	Mortality (n=10)	*p-value***	OR	95% IC	*p-value****
Recipient male sex, n (%)	60 (58.82%)	6 (60%)	0.610			
Recipient age, years (m ± SD)	46.58 ± 13.48	59.30 ±12.18	**0.005**	1.10	1.02-1.20	**0.014**
Donor male sex, n (%)	32 (31.37%)	1 (10%)	0.223			
Donor age, years (m ± SD)	55.78 ± 9.94	61.63 ± 7.46	0.107			
ABOi vs All non-DES KPD, n (%)			**0.021**			
ABOi	60 (58.82%)	2 (20%)				
All non-DES KPD	42 (41.18%)	8 (80%)				
ABOi vs KPD*ABOi (n=81) , n (%)			**0.007**	11.07	1.61-75.91	**0.014**
ABOi	60 (58.82%)	2 (20%)				
KPD*ABOi	14 (13.73%)	5 (50%)				
Immune risk*, n (%)	30 (29.41%)	6 (60%)	0.056			
Diabetes, n (%)	17 (16.67%)	3 (30%)	0.253			
BMI, kg/m²	23.40 ± 3.67	23.85 ± 3.33	0.760			
Induction, n (%)			0.561			
Pre-Transplant status, n (%)			0.168			
Pre-Tx renal replacement therapy, n (%)			0.297			
Previous transplants, n (%)	25 (24.51%)	4 (40%)	0.238			
Dialysys vintage, days, m [IQR]	543.56 [71.5-749.5]	631.60 [141-900]	0.533			

*Immune risk composite variable including previous transplant, transfusión, pregnancies, cPRA, and DSAs

**Univariant análisis (X2, T de Student, U de Mann-Whitney) ***Multivariant análisis (logistic regresion)

Results I. D-C graft survival in the final LDKT study cohort (2013-2020; n=112)

Survival estimation 320,3 months (DE: 24,9)
(300,1-397,3 95%CI)

Results I. D-C graft survival in the final LDKT study cohort (2013-2020; n=112)

	Survival (n=98)	D-C GL (n=14)	*Univariant p*	*HR****	*95% CI****	*Cox-R p****
Recipient age, m±SD	46,58 ± 13,48	59,30 ± 12,17	**0.005**			
Immune risk*, n (%)	27 (27,6%)	9 (64,3%)	**0.009**	5,413	1,579-18,558	**0,007**
Previous transplant, n(%)	22 (22,5%)	7 (50%)	**0.003**			
All kind of acute rejection, n (%)**	23 (23,47%)	7 (50%)	**0.043**	3,887	1,140-13,247	**0,030**
Cumulated dialysis vintage Mo, m±SD	62,83 ± 112,79	113,46 ± 149,07	0.053			
ABOi vs KPD, n (%)			**0.031**			
ABOi	58 (59,2%)	4 (28,6%)				
KPD	40 (40,8%)	10 (71,4%)				
ABOi vs KPD*ABOi, n (%)			0.204			
ABOi	58 (59,2%)	4 (28,6,2%)				
KPD*ABOi	16 (16,3%)	3 (21,4%)				

*   Immune risk variable included previous transplant, transfusión, pregnancies of DSAs

**   All kind of acute rejection included all types of rejection except chronic rejection

*** COX-regression (number of cases and 7 events in total of 112)

Results II. ABOi versus all- KPD (non-DES all-KPD)

Direct ABOi

Non-DES all- KPD

Total LDKT
(2006-2020; n=772)

Excluded 2006-2012 (n=326) - potential confusión factor
due to ABOi inclusions in KPD
Excluded 2021-2022 due to not-enough time of FU

LDKT cohort
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Excluded (n=19) due PCM or DES by other reasons

Mean FU
69.51±32 (0.4-123) moths

Final LDKT study cohort
(2013-2020; n=112)

ABOi
(n=62; 55,4%)

Non-DES all KPD
(n=50; 44,6%)

Time KEP inclusion – KPD transplant
12.58±13.96 (0.53-60.9) moths

Results II. ABOi versus all- KPD (non-DES all-KPD)

	ABOi (n=62)	All non-DES KPD (n=50)	p-value**
Recipient male sex, n (%)	**45 (72.58%)**	**21 (42%)**	**0.001**
Recipient age, years (m ± SD)	45.58 ±14.53	50.36±12.50	0.068
Diabetes, n(%)	9 (14.52%)	11 (22%)	0.217
BMI, kg/m²	23.72 ± 3.99	23.15 ± 3.17	0.544
Donor male sex, n (%)	16 (25.81%)	17 (34%)	0.117
Donor age, years (m ± SD)	55.08 ± 10	57.82 ± 9.56	0.160
Ethiology of Chronic kiney disease			0.718
Pre-Tx renal replacement therapy, n (%)			0.386
Pre-Transplant status, n (%)			0.337
Dialysys vintage, days, m [IQR]	**420.14 [37-580.5]**	**738.35 [302-1071]**	**0.013**
Immune risk*, n (%)	**13 (20.97%)**	**23 (46%)**	**0.004**
Inducction, n (%)			**<0.001**
None	0	2 (4%)	
Basiliximab	39 (62.9%)	10 (20%)	
Thymoglobulin / ATeGe	23 (37.10%)	38 (76%)	
Previous transplants, n (%)	**11 (17.74%)**	**18 (36%)**	**0.024**
Follow-up time, months (m ± SD)	71.86 ± 31.96	66.60 ± 32.14	0.390

*Immune risk composite variable including previous transplant, transfusión, pregnancies, cPRA, and DSAs
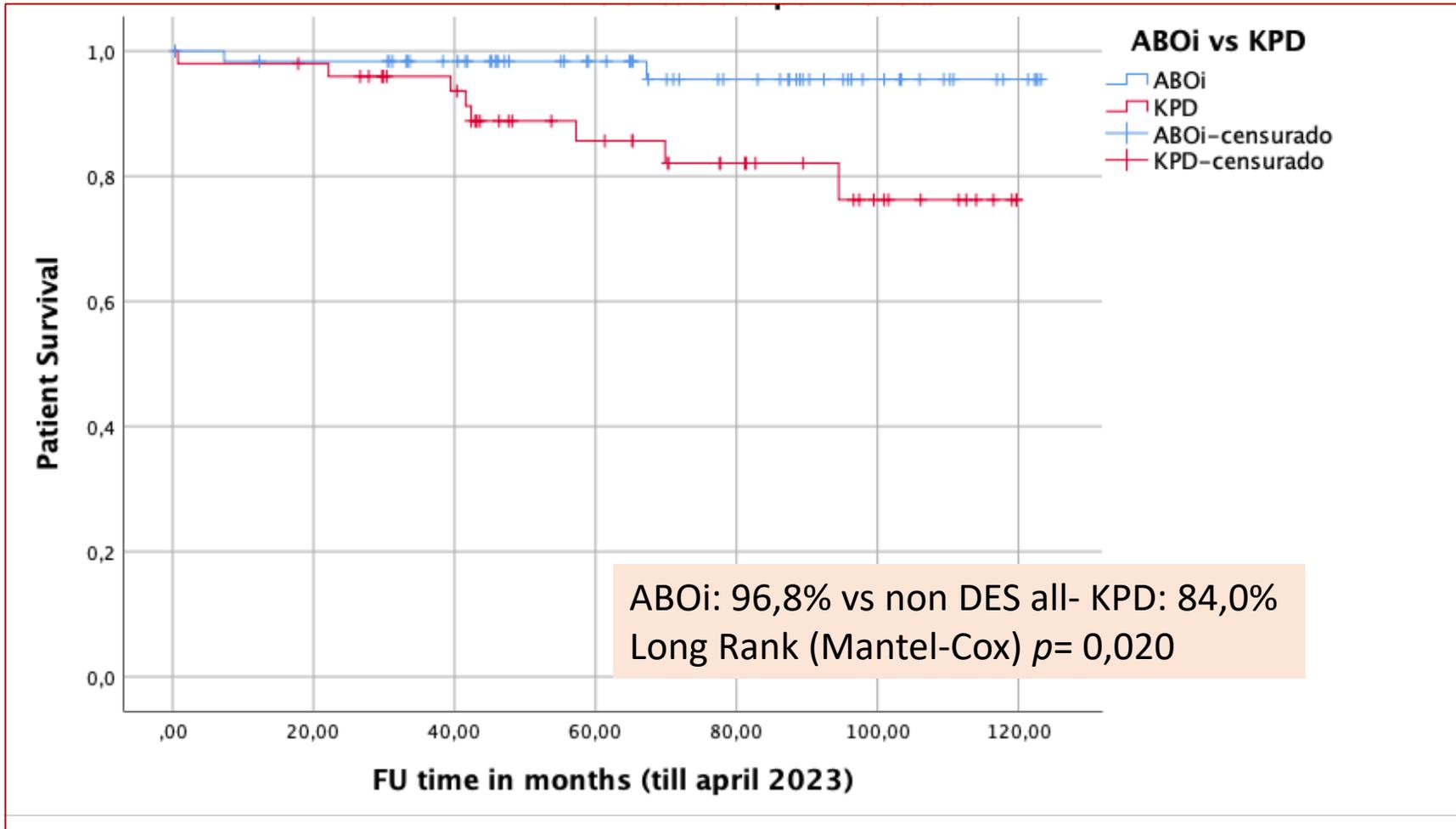
**Univariant análisis (X2, T de Student, U de Mann-Whitney)

Results II. ABOi versus all- KPD (non-DES all-KPD)

	ABOi (n=62)	All non-DES KPD (n=50)	p-value*
All kind of acute rejection, n (%)	25 (40.32%)	20 (40%)	0.564
Borderline rejection, n (%)	9 (14.52%)	8 (16%)	0.516
Antibody-mediated rejection, n (%)	10 (16.13%)	9 (18%)	0.494
Graft loss, n (%)	**7 (11.29%)**	**17 (34%)**	**0.004**
Death-censored graft loss, n (%)	5 (8.06%)	9 (18%)	0.098
Ethiology of Graft loss (n=24), n (%)			**0.036**
Death	2 (3.23%)	8 (16%)	
Interstitial fibrosis and tubular atrophy	1 (1.61%)	0	
Chronic antibody mediated rejection	1 (1.61%)	9 (18%)	
Hyperacute rejection	1 (1.61%)	0	
Thrombosis	1 (1.61%)	0	
Glomerulonephritis recurrence	1 (1.61%)	0	
Time to graft loss, months, m [IQR]	36.73 [9.81-50.45]	55.04 [27.83-81.18]	0.172
Age at graff loss, years (m ± SD)	50.30 ± 15.49	58.80 ± 13.01	0.294
Time to back to dialysis, months, m [IQR]	36.51 [12.29-33.64]	56.83 [26.61-95.59]	0.327
Mortality, n(%)	**2 (3.23%)**	**8 (16%)**	**0.021**
Time to mortality, months (m ± SD)	37.29 ± 42.37	45.98 ± 28.64	0.729
Age at mortality, years, m [IQR]	64.22 [55.25-73.19]	65.92 [59.15-72.84]	1.000

*Univariant análisis (X2, T de Student, U de Mann-Whitney)

Results II. ABOi versus all- KPD (non-DES all-KPD). Patient Survival

ABOi: 96,8% vs non DES all- KPD: 84,0%
Long Rank (Mantel-Cox) *p*= 0,020

Estimated survival for ABOi: 119,7 months
(2,448) (114.89-124.5)
Estimated survival for all-PD: 104,5 months
(4,892) (94,9-114,1)

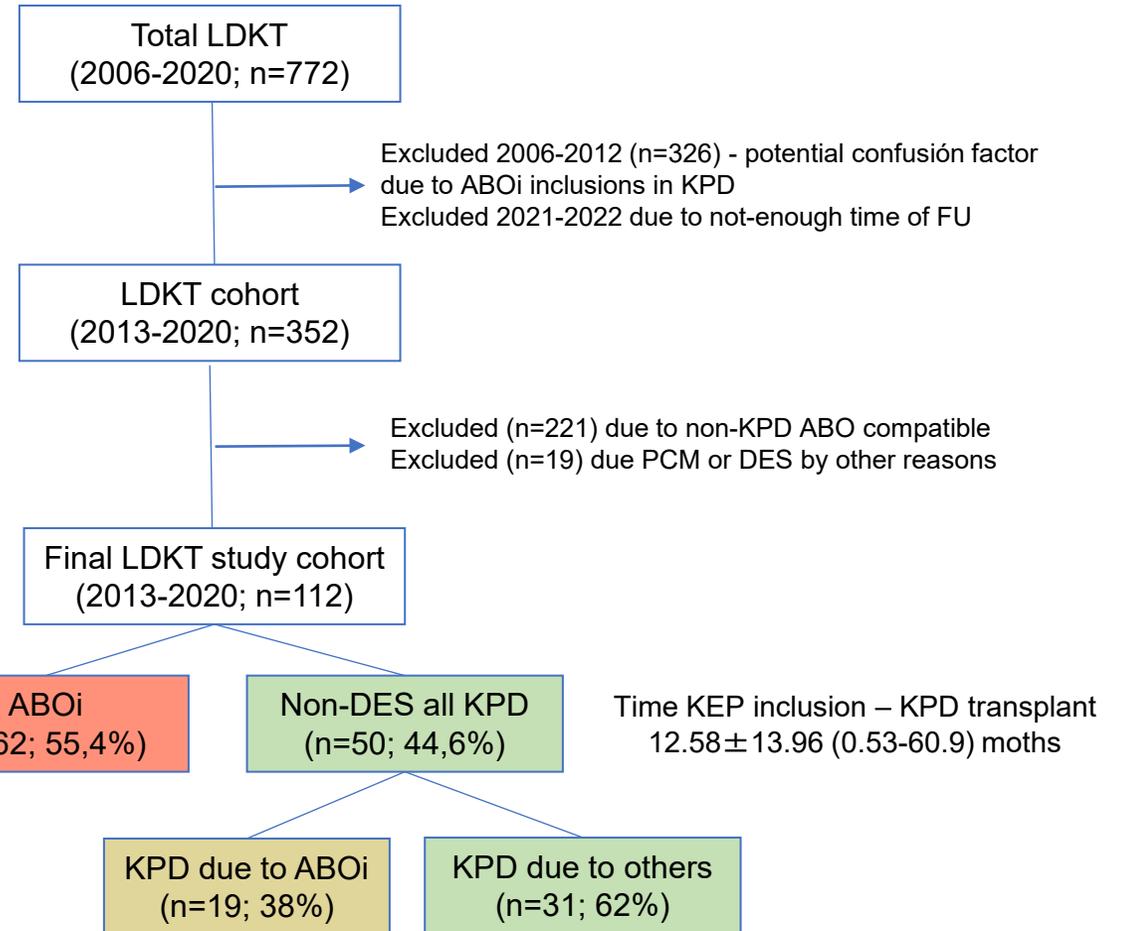# Results III. ABOi vs KPD with ABOi as program entering inclusion criteria

Direct ABOi

KPD with ABOi as program entering inclusion criteria (KPD*ABOi)

Total LDKT
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KPD due to ABOi
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KPD due to others
(n=31; 62%)

Results III. ABOi vs KPD with ABOi as program entering inclusion criteria

	ABOi (n=62)	KPD*ABOi (n=19)	*p-value**
Recipient male sex, n (%)	45 (72.58%)	12 (63.2%)	0.303
Recipient age, years (m ± SD)	45.58 ±14.53	50.42±13.68	0.202
Diabetes, n(%)	9 (14.52%)	2 (10.5%)	0.497
BMI, kg/m²	23.72 ± 3.99	22.8 ± 4.2	0.544
Donor male sex, n (%)	16 (25.81%)	13 (68.4%)	0.412
Donor age, years (m ± SD)	55.08 ± 10	56.6 ± 10.9	0.564
Ethiology of Chronic kiney disease			0.880
Pre-Tx renal replacement therapy, n (%)			0.471
Pre-Transplant status, n (%)			0.350
Dialysys vintage			0.465
Immune risk*, n (%)	13 (20.97%)	5 (26.3%)	0.419
Inducction, n (%)			0.018
None	0	2 (10.5%)	
Basiliximab	39 (62.9%)	8 (42.1%)	
Thymoglobulin / ATeGe	23 (37.10%)	9 (47.4%)	
Previous transplants, n (%)	11 (17.74%)	3 (15.8%)	0.955
Follow-up time, months (m ± SD)	71.86 ± 31.96	71.2 ± 31.9	0.911

Immune risk composite variable including previous transplant, transfusión, pregnancies, cPRA, and DSAs
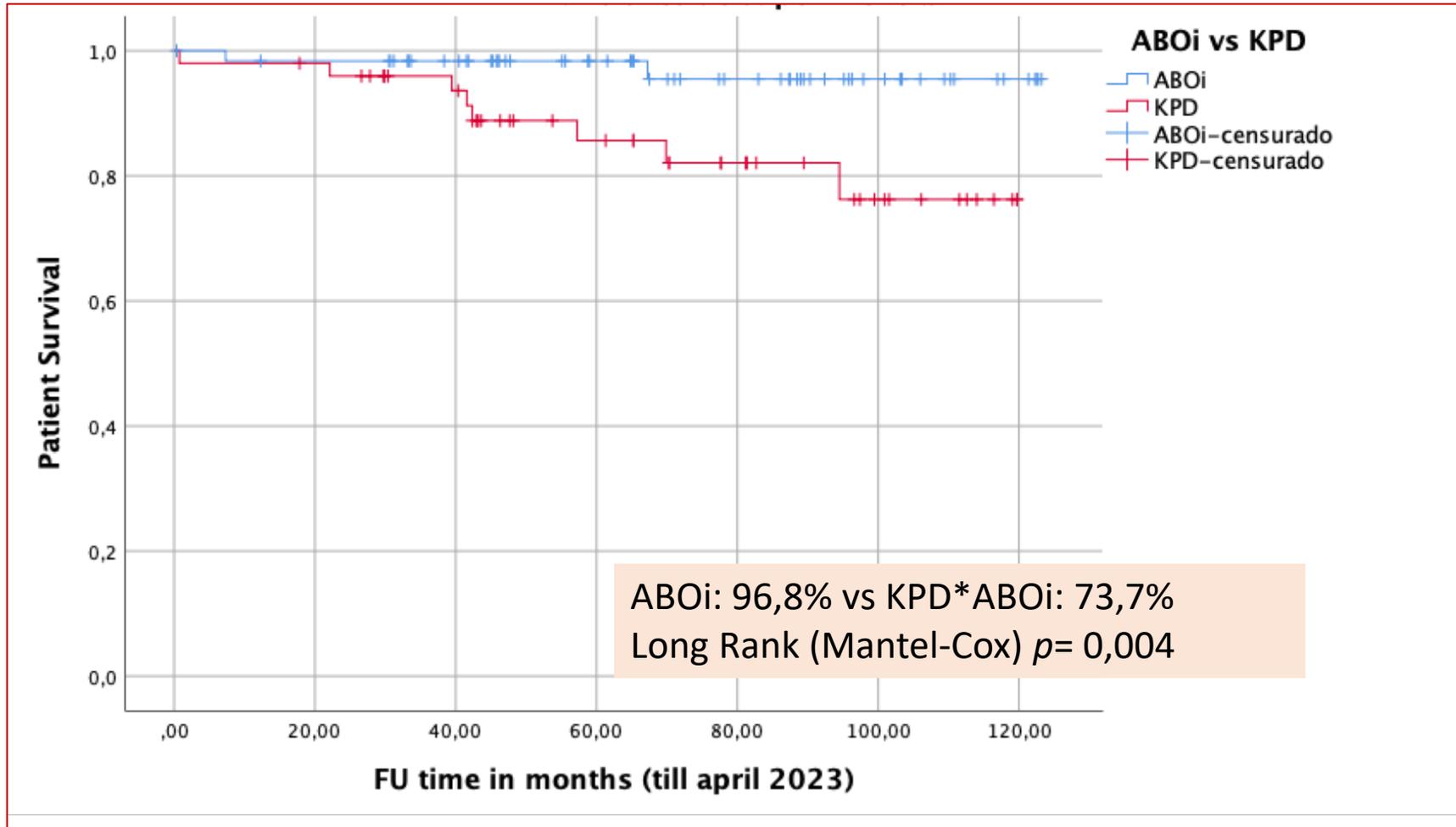
**Univariant análisis (X2, T de Student, U de Mann-Whitney)

Results III. ABOi vs KPD with ABOi as program entering inclusion criteria

	ABOi (n=62)	KPD*ABOi (n=19)	p-value*
All kind of acute rejection, n (%)	25 (40.32%)	7 (36.8%)	0.547
Borderline rejection, n (%)	9 (14.52%)	3 (15.8%)	0.573
Antibody-mediated rejection, n (%)	10 (16.13%)	2 (10.5%)	0.427
Graft loss, n (%)	7 (11.29%)	7 (36.8%)	0.016
Death-censored graft loss, n (%)	5 (8.06%)	2 (10.5%)	0.523
Ethiology of Graft loss			0.345
Time to graft loss, months, m [IQR]			0.109
Mortality, n(%)	**2 (3.23%)**	**5 (26.3%)**	**0.007**
Ethiology of Mortality			**0.072**
Time to mortality, months			0.983

*Univariant análisis (X2, T de Student, U de Mann-Whitney)

Results III. ABOi vs KPD with ABOi as program entering inclusion criteria. Patient survival

ABOi: 96,8% vs KPD*ABOi: 73,7%
Long Rank (Mantel-Cox) *p*= 0,004

Estimated survival for ABOi: 119,7 months (2,448) (114.89-124.5)
Estimated survival for KPD*ABOi: 97,1 months (8,999) (79,4-114,7)

Summary and conclusions

- **Worst patient and death-censored graft survival in non-DES all KPD than ABOi LDKT**, with different immune risk composite variable, *de novo* immunosuppressive therapy, and cumulative dialysis vintage between both groups

- Comparing **direct ABOi with KPD with ABOi as program entering inclusion criteria, only worst patient survival** was observed, without specific immune profile of patients except by different *de novo* immunosuppressive therapy

- In our serie, <u>**recipient age and the option of direct ABOi and KPD with ABOi as program entering inclusion criteria were associated with patient survival**</u>. Then, in aging patients, direct ABOi LDKT could be a suitable option in detriment to KPD, despite the considering impact of DES in this kind of patient

More granularity in the analysis needs to be done in order to identify such associated variables for the patient survival prediction, and to facilitate the decision to offer a direct ABOi LDKT or to go to the KPD transplant

Management coordinator of LDKT program

Patient Management ICNU department

Department of Nephrology and Kidney Transplant

Advanced Role Nursing team

Aphreresis Therapy Unit

Department of Urology and Kidney Transplant

Anesthersiology

Coordination Unit

Urology Nurse team

Radiologist

Immunology

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Medical director of LDKT program