ABO incompatible kidney transplantation

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Sarajevo 2017

Objectives

- Why a transplant?
- What kind of transplant?
- Current status
- Other options?
- ABO incompatibility
- History
- Current practice
- Complications
- Outcomes
- General considerations

Mortality rates for patients on dialysis, patients listed for transplantation, and transplant recipients

All RRT Patients		Waiting List		Transplant Group	
N	Death Rate	N	Death Rate	N	Death Rate
4532	24.30	1736	9.02	1095	4.13

Relative risk of mortality over time after transplantation versus dialysis patients on the waiting list

All Patients	<30 days	31 to 365 days	>365 days
No comorbidity adjustment	1.35 (0.63 to 2.86)	0.67 (0.48 to 0.95)*	0.32 (0.25 to 0.40)*
Comorbidity adjusted	0.91 (0.22 to 3.70)	0.50 (0.28 to 0.90)*	0.28 (0.20 to 0.39)*

Impact of Cadaveric Renal Transplantation on Survival in Patients Listed for Transplantation.
GC Oniscu et al J Am Soc Nephrol 2005 16:1859-1865.

Projected years of life for patients on dialysis and transplant recipients from the moment of listing for transplantation

All Patients	Years of Life on Dialysis	Years of Life with a Kidney Transplant
Male	5.84	17.19
Female	5.63	16.13
Primary renal disease	5.99	16.98
Glomerulonephritis	6.37	17.40
Interstitial nephritis	8.90	21.31
Multisystem disease	5.39	14.16
Diabetes	2.92	8.60
Other	5.36	12.27
Age, yr		
18 to 34	27.22	41.50
35 to 49	6.71	18.03
50 to 59	5.12	11.18
60 to 64	4.32	7.84
≥65	3.69	7.60

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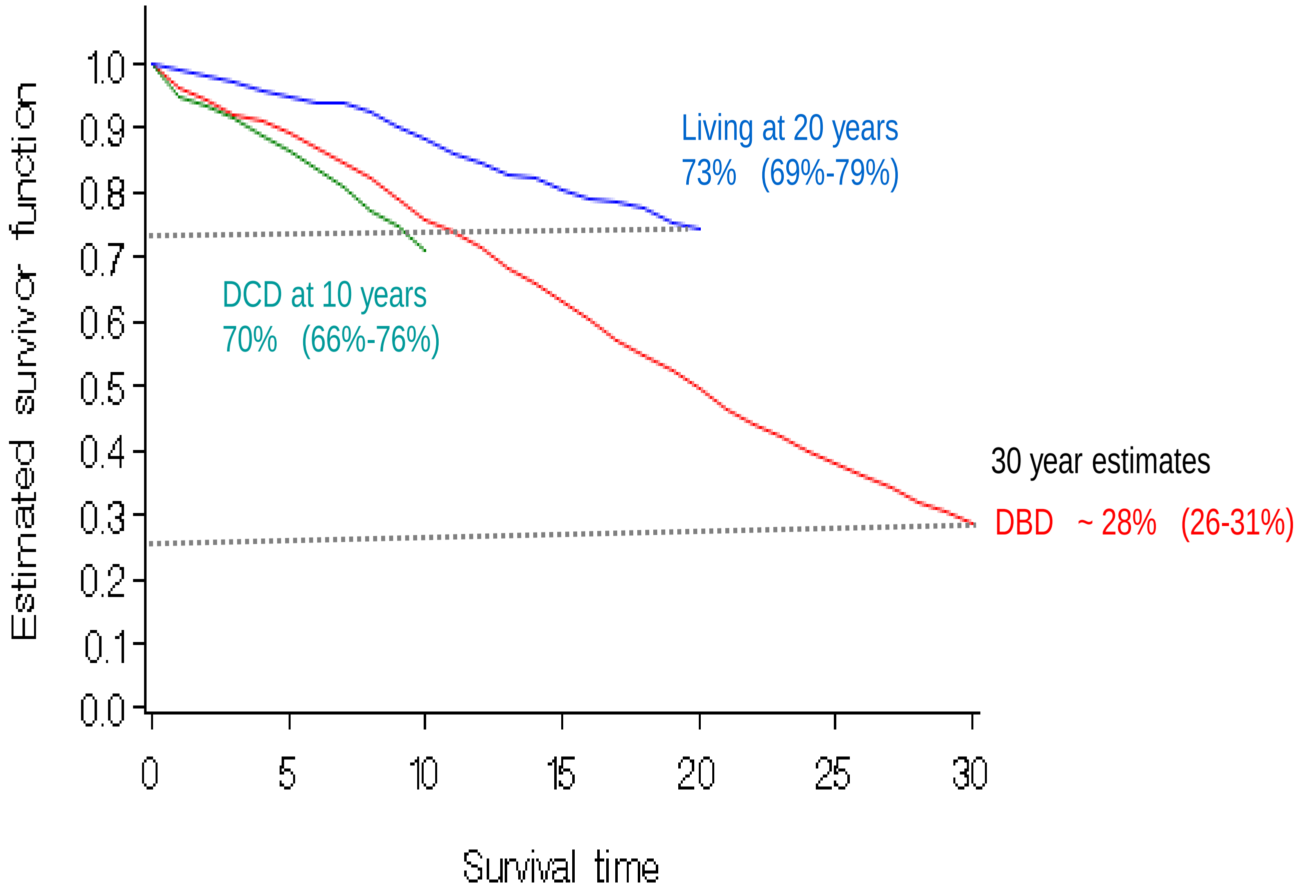
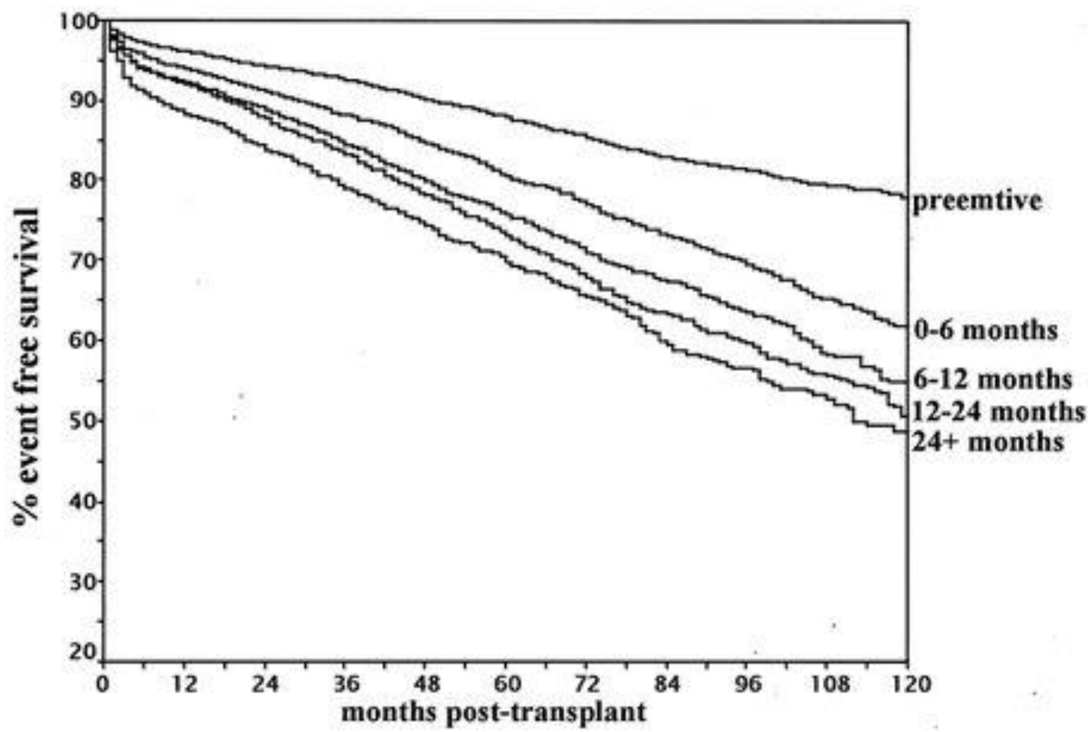
Patient survival, by donor type
(censoring non-fatal graft failure)



Observation window: 2010 to 2012

Early better than late?

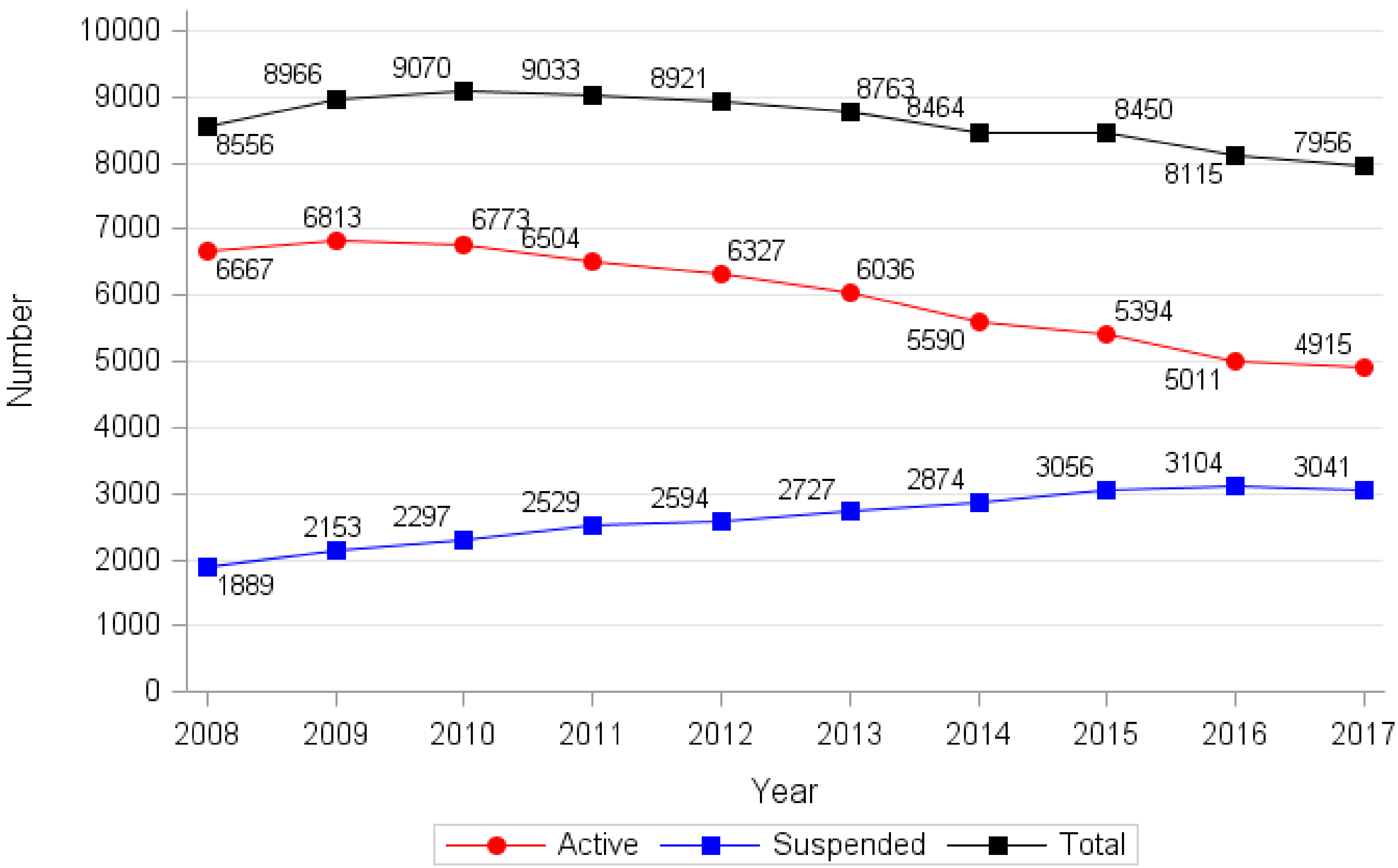


Unadjusted graft survival in 21,836 recipients of living transplants by length of dialysis treatment before transplant.

Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: A Paired Donor Kidney Analysis. Meier-Kriesche, H-U et al Transplantation 2002 74:1377-1381

NHS Blood and Transplant

Figure 3.1 Adult patients on the kidney only transplant list at 31 March



Source: Annual Report on Kidney Transplantation 2016/17, NHS Blood and Transplant

Figure 3.10 Median waiting time to deceased donor transplant for adult patients registered on the kidney transplant list, 1 April 2011 - 31 March 2014

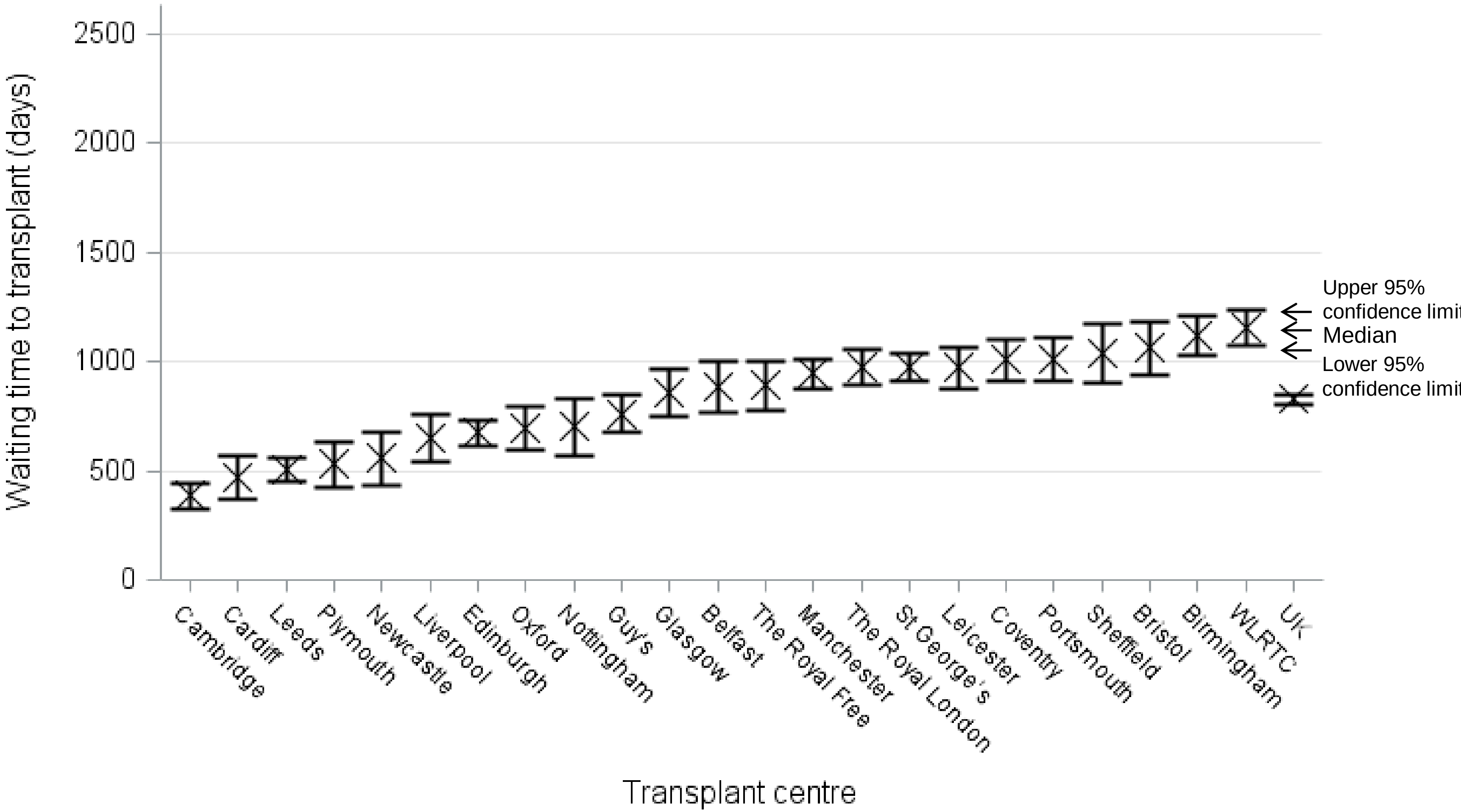
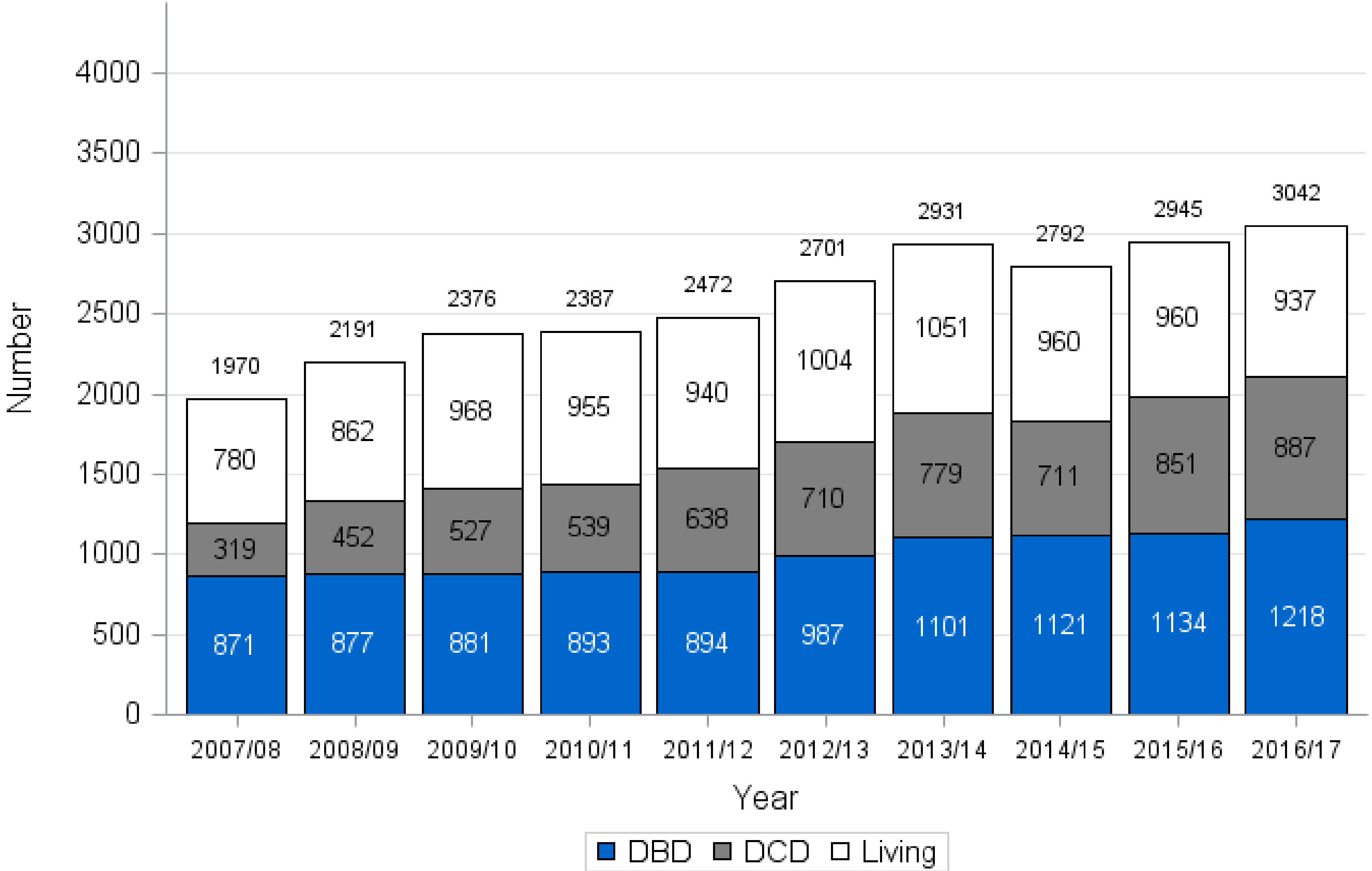


Figure 5.1 Adult kidney only transplants, 1 April 2007 - 31 March 2017



Pre-emptive kidney transplantation - UK

Figure 5.5 Adult deceased donor pre-emptive transplant rates by centre, 1 April 2015 - 31 March 2016

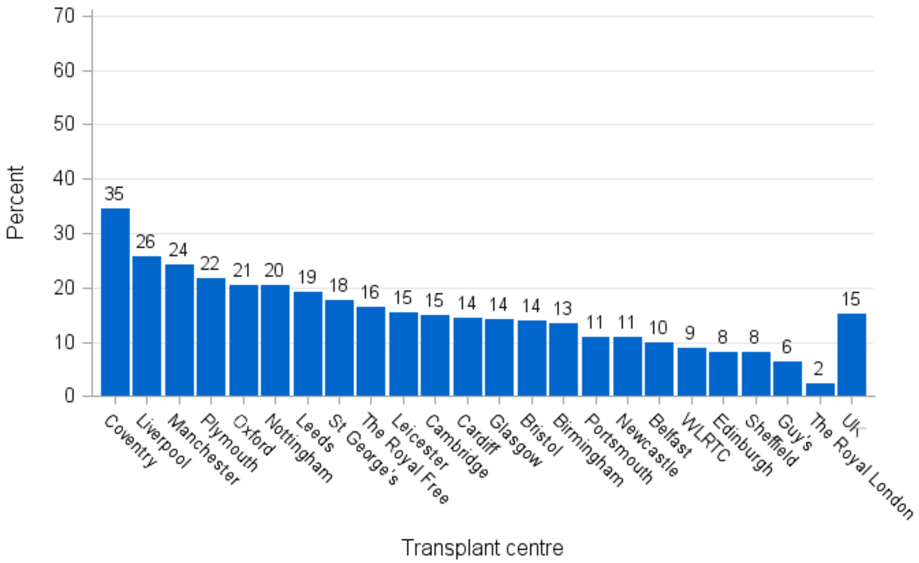
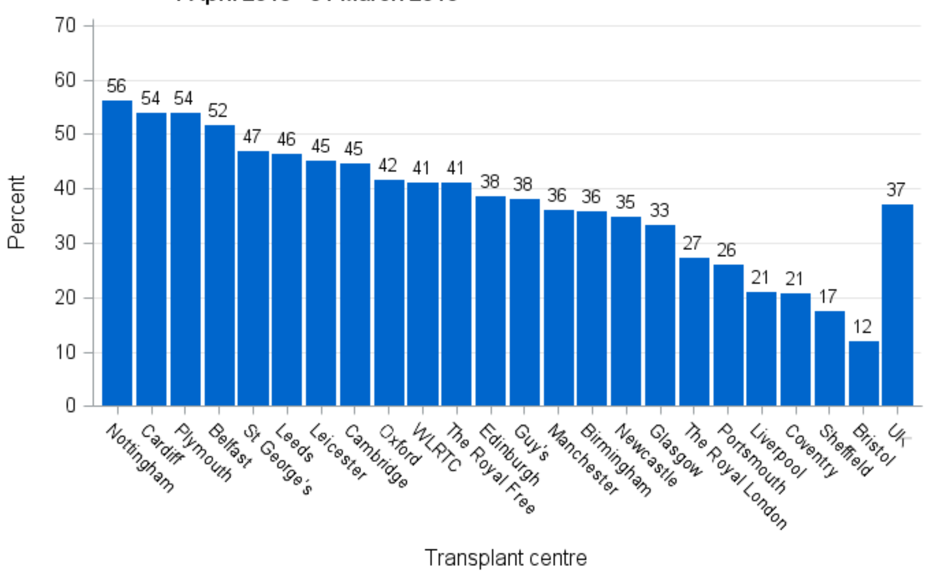
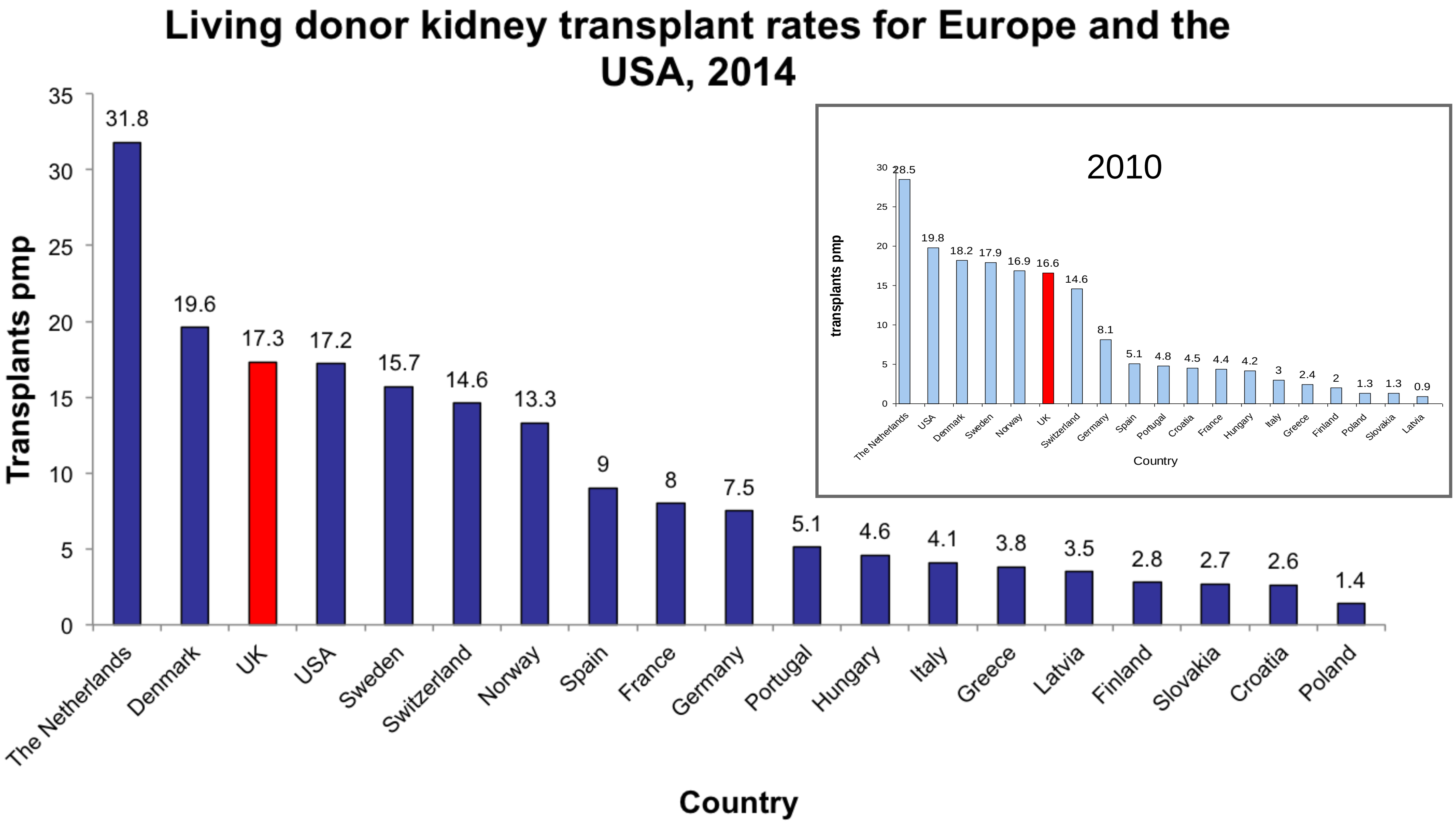


Figure 5.6 Adult living donor pre-emptive transplant rates by centre, 1 April 2015 - 31 March 2016



International data - living donor (LD) kidney transplant rates



The Potential for Paired Living Kidney Donation in the UK

RJ Johnson, JE Blackwell, L Burnapp, DC Pugh, SV Fuggle, CJ Rudge

On behalf of the UK Transplant Kidney and Pancreas Advisory Group, UK Transplant, Bristol, BS34 8RR, United Kingdom

ABO incompatibility and the presence of donor-specific HLA antibody preclude many potential living donor kidney transplants. From April 2006, the Human Tissue Act will enable paired donation in the UK, whereby incompatible donor-recipient pairs can exchange kidneys so that recipients can receive alternative compatible living donor organs. This study aims to identify the potential for establishing a paired kidney donation scheme in the UK.

All transplant centre based UK living donor transplant co-ordinators were contacted in Autumn 2005 and asked to provide data on living donor kidney transplants that could not proceed because of ABO or HLA incompatibility.

Information received from 13 centres relating to the last 2 years (290 pairs) showed 46% of potential donor-recipient pairs were ABO incompatible and 54% were HLA incompatible.

The demographics of the potential recipients were - age 43±1.5 years, 53% female, 87% white. 20% were incompatible with more than one prospective donor. 61% of the potential recipients are on the deceased donor transplant list, 13% have received a deceased donor transplant and 3% have received an alternative living donor transplant. The mean age of the prospective donors was 44±1.5 years and 32%, 28% and 19%, respectively, were spouse/partners, siblings or parents of the potential recipients. Blood group distributions of the potential recipients and their donors are different from those in normal donor and recipient pools, as shown below, and suggest that too few blood group O donors will be available to meet demand.

To inform discussion on the complex issues surrounding the establishment of a paired kidney donation scheme, the data collected will be used in computer simulation models developed to compare and contrast the effectiveness of alternative matching algorithms.

	Donor blood group (%)				Recipient blood group (%)			
	O	**A**	**B**	**AB**	**O**	**A**	**B**	**AB**
Blood group incompatible	0	61	27	12	79	11	10	0
HLA incompatible	62	29	8	1	38	41	17	4
All	33	44	17	6	57	28	14	2
Deceased donors/Tx list	48	39	10	2	50	33	14	3

NHS Blood and Transplant

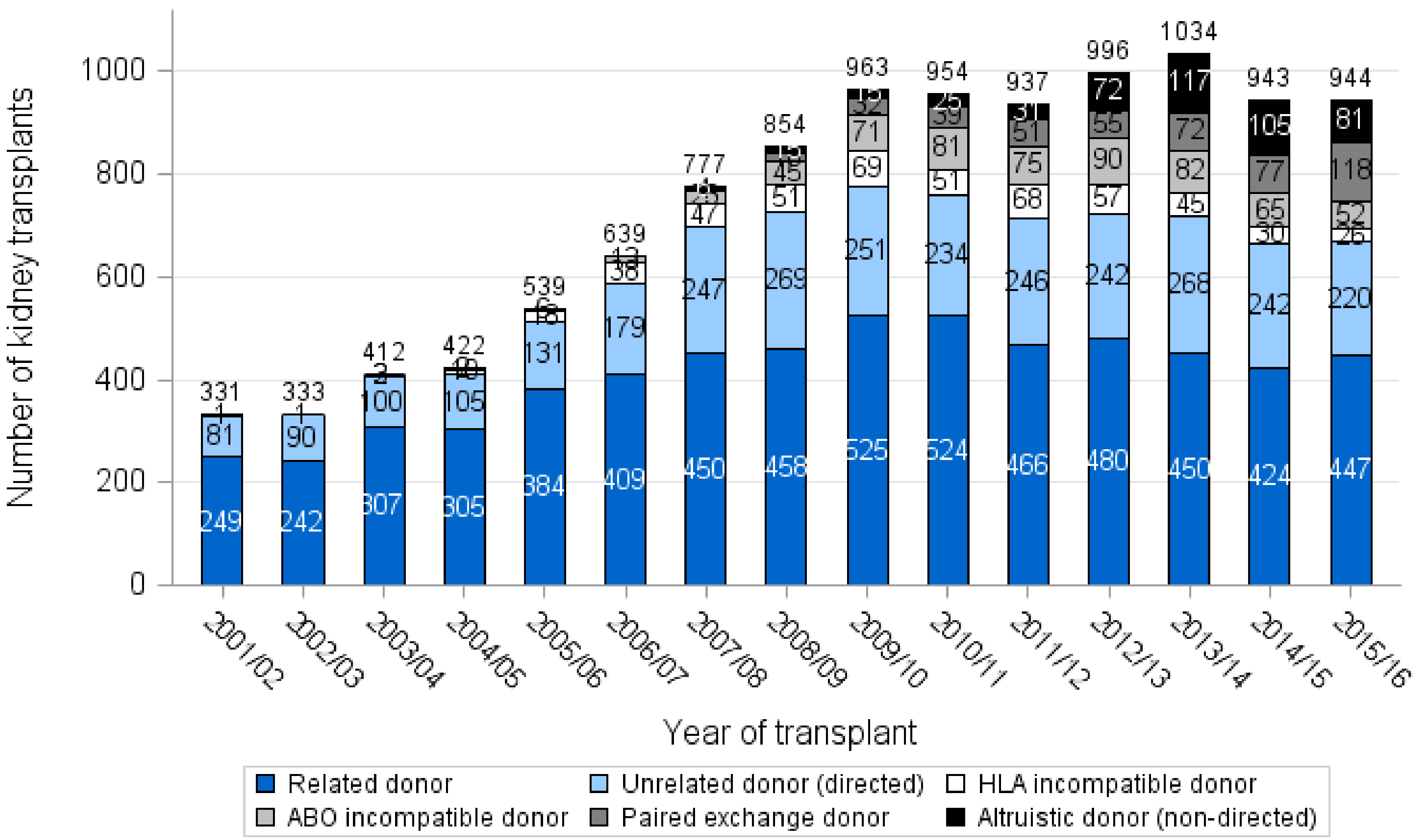
National Living Donor Kidney Sharing Schemes (NLDKSS)

Include:

- Paired/pooled donation (PPD)
- Non-directed altruistic donation (NDAD)
- Altruistic Donor Chains (ADC)

Adult living donor transplants

Increasing complexity of living donor kidney transplantation



Transplant rates – by ABO of registered pairs (to Apr 2012)

NHS Blood and Transplant

Recipient ABO

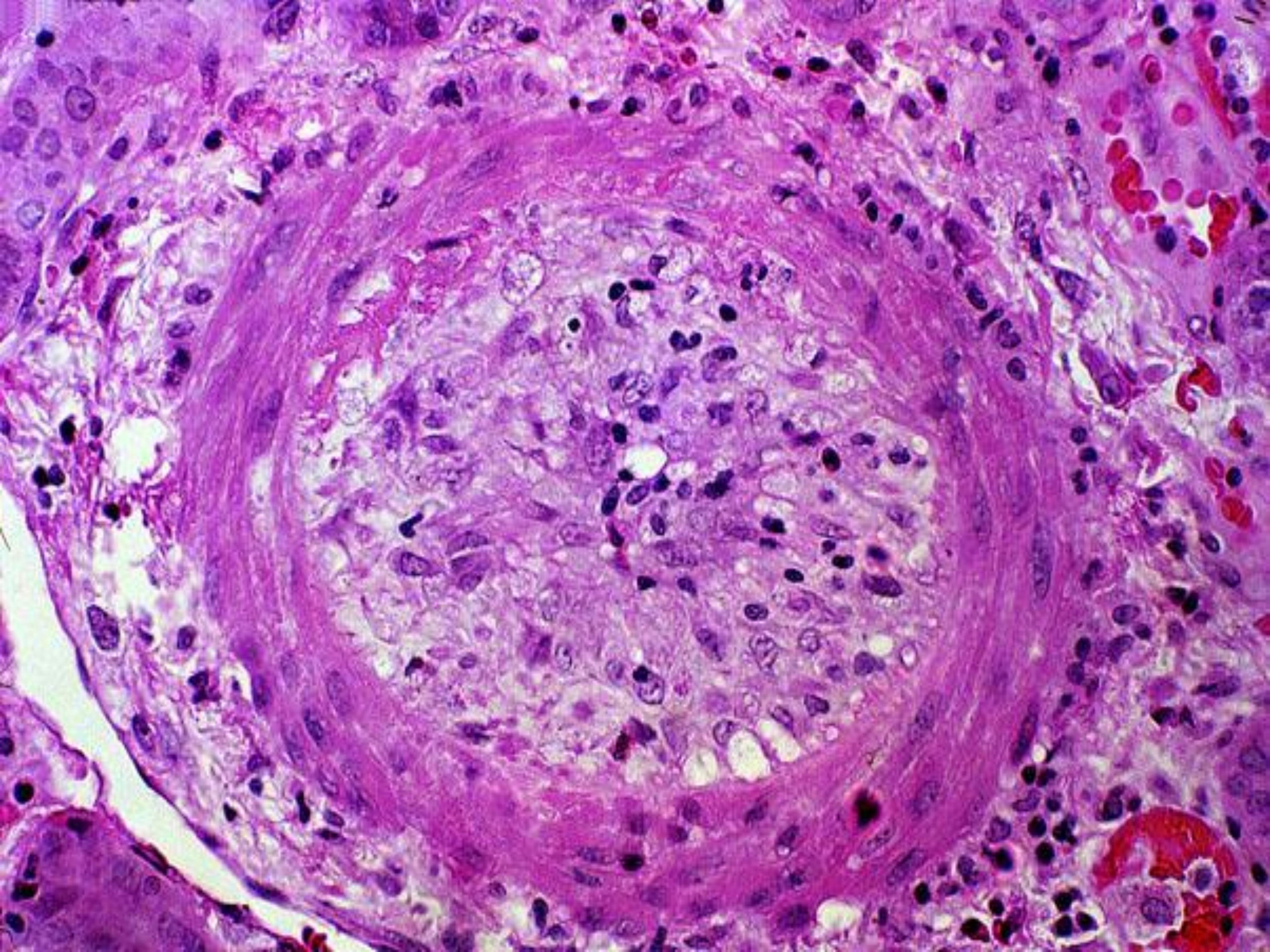
Donor ABO	O	A	B	AB
O	31/145 (21%)	33/62 (53%)	9/26 (33%)	2/3 (67%)
A	34/213 (16%)	17/75 (23%)	13/42 (31%)	0/5 (0%)
B	10/59 (17%)	12/32 (38%)	2/22 (9%)	1/4 (25%)
AB	0/10 (0%)	0/3 (0%)	0/9 (0%)	0/2 (0%)

Number transplanted / number enrolled (%)

Altruistic donor chains are excluded

ABO incompatibility

- ABO Gene on Chromosome 9
- Blood group inherited quite separately to HLA
- Blood group O (45%)
- Blood group A (40%)
- Blood group B (11%)
- Blood group AB (4%)
- ABO gene products are glycoprotein chains
- Antibodies directed against A and B probably occur through B-cell recognition of gut bacteria
- Individuals then produce antibodies against non-self glycoprotein chains
- Early experience suggested that these antibodies could cause hyperacute rejection and allograft thrombosis



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Ota *et al*[21]	Observational, comparative	51	51	DFPP and/or IAs/SPx	2-yr graft survival: 87% *vs* 84.6% *vs* 50% (A- *vs* B- *vs* ABO-incompatible)
Tanabe *et al*[22]	Observational, comparative	433	67	DFPP and IAs/SPx	8-yr graft survival: 73% *vs* 80 % (ABOi *vs* ABOc)
Ishida *et al*[23]	Observational	93	93	DFPP/SPx	5-yr graft survival: 73%
Ohta *et al*[24]	Observational, pediatric	10	10	DFPP or PE or IAs/SPx	5.4-yr graft survival: 100%
Shishido *et al*[25]	Observational, pediatric	16	16	PE and IAs/SPx	5-yr graft survival: 85%
Takahashi *et al*[2]	Observational, comparative	1496	441	DFPP or PE or IAs/SPx	9-yr graft survival: 59% *vs* 57% (ABOi *vs* ABOc)
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Wilpert *et al*[34]	Observational, comparative	83	40	IAs/RIT/IVIG	Graft survival: ABOi 100% (3.3-yr) *vs* ABOc 93% (1.5-yr)
Tyden *et al*[1]	Observational, comparative, pediatric	38	10	IAs/RIT/IVIG	Graft loss within 3 years: ABOi 1 case, ABOc 2 cases
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Table 1. Related ABO-Incompatible Living Donor Renal Allograft With Splenectomy of the Recipient

No.	Age	Donor	ABO Incompatibility	RhD*	RhR†	Follow-up (months)	Serum Creatinine (mg %)
1	18	Mother	A_1 to O	+	+	58	1.25
2	13	Mother	A_1 to O	+	+	53	0.84
3	24	Mother	A_1 to O	+	+	53	1
4	17	Mother	B to O	+	−	52	1.22
7	31§	Mother	B to O	+	+	41	1.46
8	27	Sister	B to O	+	+	40	1.8
9	20	Mother	A_1B to B	+	+	35	1.96
10	9	Mother	A_1 to B	+	+	Chronic rejection	
11	33	Mother	A_2 to O	+	−	33	1.7
12	10	Father	A_1 to O	+	+	31	0.95
13	19	Mother	A_1 to O	−	+	Acute irreversible rejection after 1 week	
15	17	Father	A_1 to O	+	+	25	1.64
17	11	Mother	A_1 to O	+	+	21	0.9
18	21	Mother	A_1B to A_1	+	+	18	1.8
21	12	Mother	B to O	+	+	11	0.92
22	11‡	Uncle	A_1 to O	+	+	7	0.71
23	12	Father	B to O	+	+	7	0.97

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Table 2. Unrelated ABO-Incompatible Living Donor Renal Allografts (Splenectomized)

No.	Sex	Donor	HLA-Antigens	ABO	Rh	Date Tr.	Follow-up
5. D	M	Husband	A 26, A 11, B 14, B 18, DR 5, DR 7	A_1	–	2-2-83	Creat.
R*	F	Wife	A 2, A 30, B 45, —, DR 5, DR 7	0	–		1.25 mg %
6. D	F	Wife	—, A 30, B 50, B 55, DR 5, DR 7	A_1	+	9-9-83	Chronic rejection
R	M	Husband	A 2, A 24, B 8, B 51, DR 3, DR 4	B	–		RD:3-27-84
14. D	F	Wife	A 32, A 23, B 27, B 49, DR 2, DR 7	A_1	+	1-23-85	Creat.
R	M	Husband	A 2, A 24, B 35, B 39, —, DRW 6	0	+		1.06 mg %
16. D	F	Wife	A 1, A 24, B 35, B 49, DR 5, DRW 6	A_1	+	6-5-85	Creat.
R	M	Husband	A 11, A 32, B 35, B 52, DR 2, DRW 6	0	+		1.9 mg %
19. D	F	Wife	—, A 2, B 44, —, DR 5, DR 7	A_1	+	12-4-85	Acute rejection
R	M	Husband	A 1, A 2, B 49, —, DR 5, DR 4	0	+		Ty 12-23-85†
20. D	F	Wife	A 23, —, B 49, B 58, DR 5, DRW 6	A_2	+	4-16-86	Death from CMV
R	M	Husband	A 28, —, B 35, B 44, DR 1, —	0	+		at 2 months

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Pre-operative plasmapheresis

ALG, Azathoprine (1mg/kg/day) , Prednisolone (0.4mg/kg/day)

ALG, Ciclosporin (Trough level 50-100ng/ml), Azathioprine, Steroids

Splenectomy either before transplantation at at the time of transplantation

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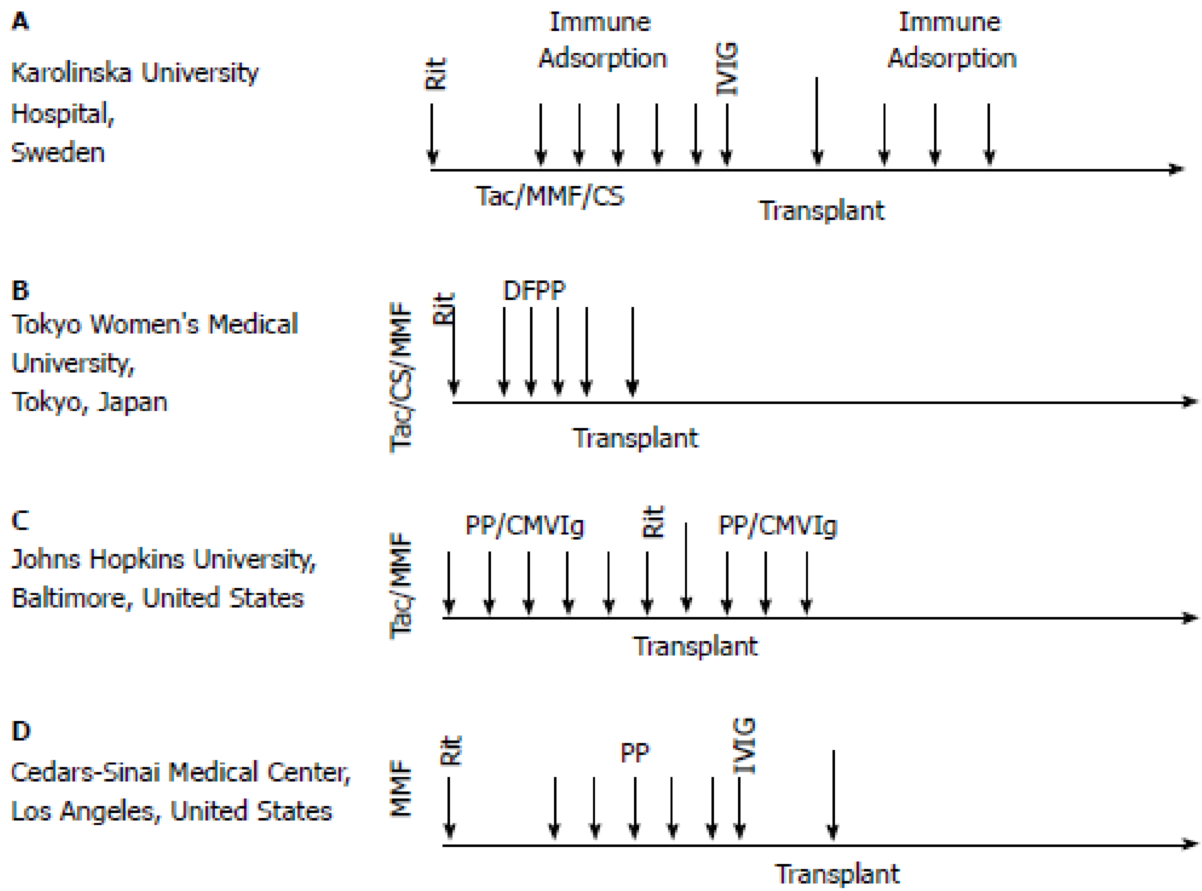
Author	Country, year	Rituximab dose	Pretransplant IS	Antibody depletion	IVIG	Target titer at the time of transplantation	Induction IS	Maintenance IS	Posttransplant antibody depletion
Adult recipients									
Rituximab protocol									
Saito *et al*[53]	Japan, 2006	375 mg/m^2 (twice) at -14 and -1 d	MMF/MP at -1 Mo	DFPP or PE	-	< 1:16	BAS (20 mg at 0 and 4 d)	CYA/MMF/MP	-
Tyden *et al*[54]	Sweden, 2006	375 mg/m^2 (once) at -1 mo	TAC/MMF/Pred at -13 d	IAs	0.5 g/kg after last IAs	< 1:8	-	TAC/MMF/Pred	IAs, 3 times
Chikaraishi *et al*[55]	Japan, 2008	100 mg/m^2 (twice) at -8 and -1 d	MMF/MP at -14 d, TAC at -3 d	DFPP and PE	-	< 1:8	BAS (20 mg at 0 and 4 d)	TAC/MMF/MP	-
Galliford *et al*[30]	United Kingdom, 2008	1000 mg (twice) at first day of PE and at the operative day	TAC/MMF at -14 d	PE	0.1 g/kg after each PE	< 1:4	DAC (2 mg/kg at 0 and 14 d)	TAC/MMF/Pred	PE at 1 and 3 d
Genberg *et al*[31]	Sweden, 2008	375 mg/m^2 (once) at -1 mo	TAC/MMF/Pred at -10 d	IAs	0.5 g/kg at -1 d	< 1:8	-	TAC/MMF/Pred	IAs, 3 times
Oettl *et al*[32]	Switzerland, 2009	375 mg/m^2 (once) at -1 mo	TAC/MMF /Pred at -14 d	IAs	0.5 g/kg after last IAs	< 1:8	BAS (20 mg at 0 and 4 d)	TAC/MMF/Pred	IAs or PE (not routinely)
Sivakumaran *et al*[78]	United States, 2009	375 mg/m^2 (once) at -3 wk	MMF at -1 mo	PE	2 g/kg after last PE	NA	ALE (1 mg/kg at 0 and 14 d)	TAC/MMF/Pred	-
Wilpert *et al*[34]	Germany, 2010	375 mg/m^2 (once) at -1 mo	TAC/MMF or MPS/ Pred at -7 d	IAs	0.5 g/kg at -1 to -5 d	< 1:4	BAS (20 mg at 0 and 4 d)	TAC/MMF/Pred	IAs (not routinely)
Fuchinoue *et al*[36]	Japan, 2011	100-1000 mg, 1-3 times	CYA or TAC/MMF at -2 d	DFPP or PE	-	< 1:16	BAS (20 mg at 0 and 4 d)	CYA or TAC/ MMF/steroid	-
Habicht *et al*[37]	Germany, 2011	375 mg/m^2 (once) at -1 mo	TAC/MMF/ Pred at -1 mo	IAs	30 g at -1 to -2 d	< 1:8	-	TAC/MMF/MP	IAs (not routinely)
Lipshutz *et al*[38]	United States, 2011	375 mg/m^2 (once) at -1 mo	TAC/MMF at the first day of PE	PE	10 g after each PE	< 1:8	ATG (1.5 mg/kg for 4 d)	TAC/MMF/Pred	PE (not routinely)
Shirakawa *et al*[39]	Japan, 2011	500 or 200 mg/m^2 (once), at -5 to -7 d	TAC/MMF/ MP at -7 d	DFPP	-	< 1:32	BAS (20 mg at 0 and 4 d)	TAC/MMF/MP	-
Morath *et al*[40]	Germany, 2012	375 mg/m^2 (once) at -1 mo	TAC/MMF/ MP at the first day of IAs	IAs	0.5 g/kg after last IAs	< 1:16	BAS (20 mg at 0 and 4 d)	TAC/MMF/MP	IAs or PE (not routinely)
Uchida *et al*[41]	Japan, 2012	150 mg/m^2 (twice) at -14 and 0 d	MMF/MP at -1 Mo, CYA or TAC at -3 d	DFPP or PE	-	< 1:16	BAS (20 mg at 0 and 4 d)	CYA or TAC/ MMF/MP	-
Rituximab-free protocol									
Montgomery *et al*[43]	United States, 2009	-	TAC/MMF at the first day of PE	PE	0.1 g/kg after each PE	< 1:16	DAC (2 mg/kg initial dose, 1 mg/ kg every 2 wk for total 5 doses)	TAC/MMF/Pred	PE, at least twice (with IVIG 0.1 g/kg)
Flint *et al*[35]	Australia, 2011	-	MMF at -10 to -14 d	PE	0.1 g/kg after each PE	< 1:8	BAS (20 mg at 0 and 4 d)	TAC/MMF/Pred	PE (not routinely)
Ashimine *et al*[42]	Japan, 2013	-	MMF at -14 d	DFPP	-	< 1:8	BAS (20 mg at 0 and 4 d)	CYA or TAC/ MMF/Pred	-
Pediatric recipients									
Genberg *et al*[31]	Sweden, 2008	375 mg/m^2 (once) at -1 mo	TAC/MMF/ Pred at -10 d	IAs	0.5 g/kg at -1 d	< 1:8	-	TAC/MMF/Pred	IAs, 3 times
Tyden *et al*[1]	Sweden, 2011[1]	375 mg/m^2 (once) at -1 mo	TAC/MMF/ Pred at -13 d	IAs	0.5 g/kg after last IAs	< 1:8	-	TAC/MMF/Pred	IAs, 3 times

World J Transplant 2014 March 24; 4(1): 18-29. Muramatsu et al

Modern approaches to incompatible kidney transplantation



World J Nephrol 2015 4(3):354-362. Wongsaroj et al

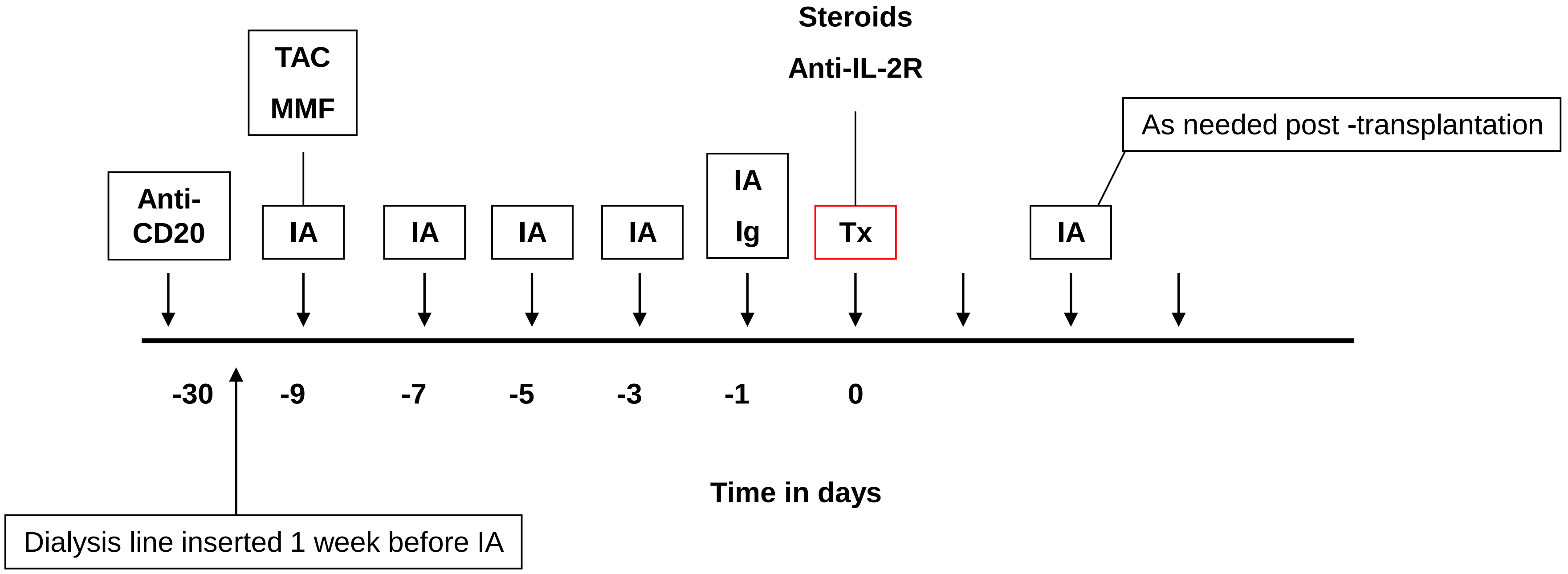
ABO Incompatible Transplantation

Table 1. Effect of antigen-specific immunoadsorption and current serum creatinine levels

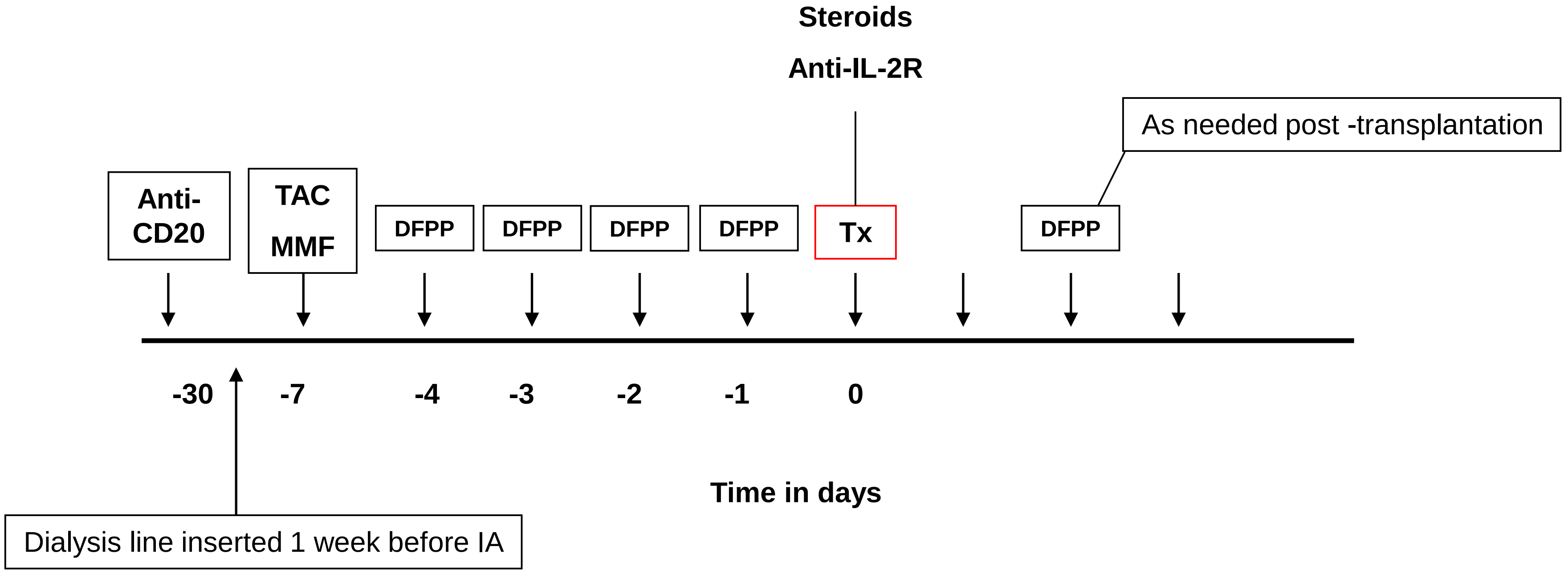
	Donor/ recipient blood groups	IgG titres before adsorptions	Number of preoperative adsorptions	IgG titres at transplant	Number of postoperative adsorptions	Follow-up months	Serum creatinine at follow-up (µmol/l)
1	A2/O	1:64	4	1:2	3	48	75
2	B/A	1:16	4	1:1	3	34	154
3	B/O	1:32	4	1:4	3	20	HD
4	A1/O	1:64	8	1:1	16	28	139
5	A2/O	1:64	4	1:4	3	27	154
6	A1/O	1:128	9	1:2	5	25	89
7	A2/O	1:64	4	1:1	2	23	0 99
8	B/A	1:8	4	1:1	3	22	120
9	B/O	1:2	0	1:2	3	17	0 22
10	A1B/B	1:16	4	1:2	6	16	103
11	A1/O	1:16	4	1:2	5	16	103
12	A1/O	1:1	0	1:1	3	14	41
13	A1B/B	1:16	4	1:1	3	8	104
14	A1/O	1:32	4	1:4	4	7	139
15	A1/O	1:32	8	1:4	4	7	139
16	B/O	1:64	5	1:2	3	6	117
17	B/O	1:64	4	1:2	3	5	131
18	A2/O	1:32	4	1:4	12	3	99
19	AB/A	1:16	4	1:2	3	2	109
20	A1/O	1:64	4	1:2	9	2	121
21	A1/O	1:32	4	1:2	3	1	138

The Stockholm experience with ABO-incompatible kidney transplantations without splenectomy. Xenotransplantation 2006;13:105-107. Tyden G et al

ABOi Transplantation protocol



ABOi Transplantation protocol



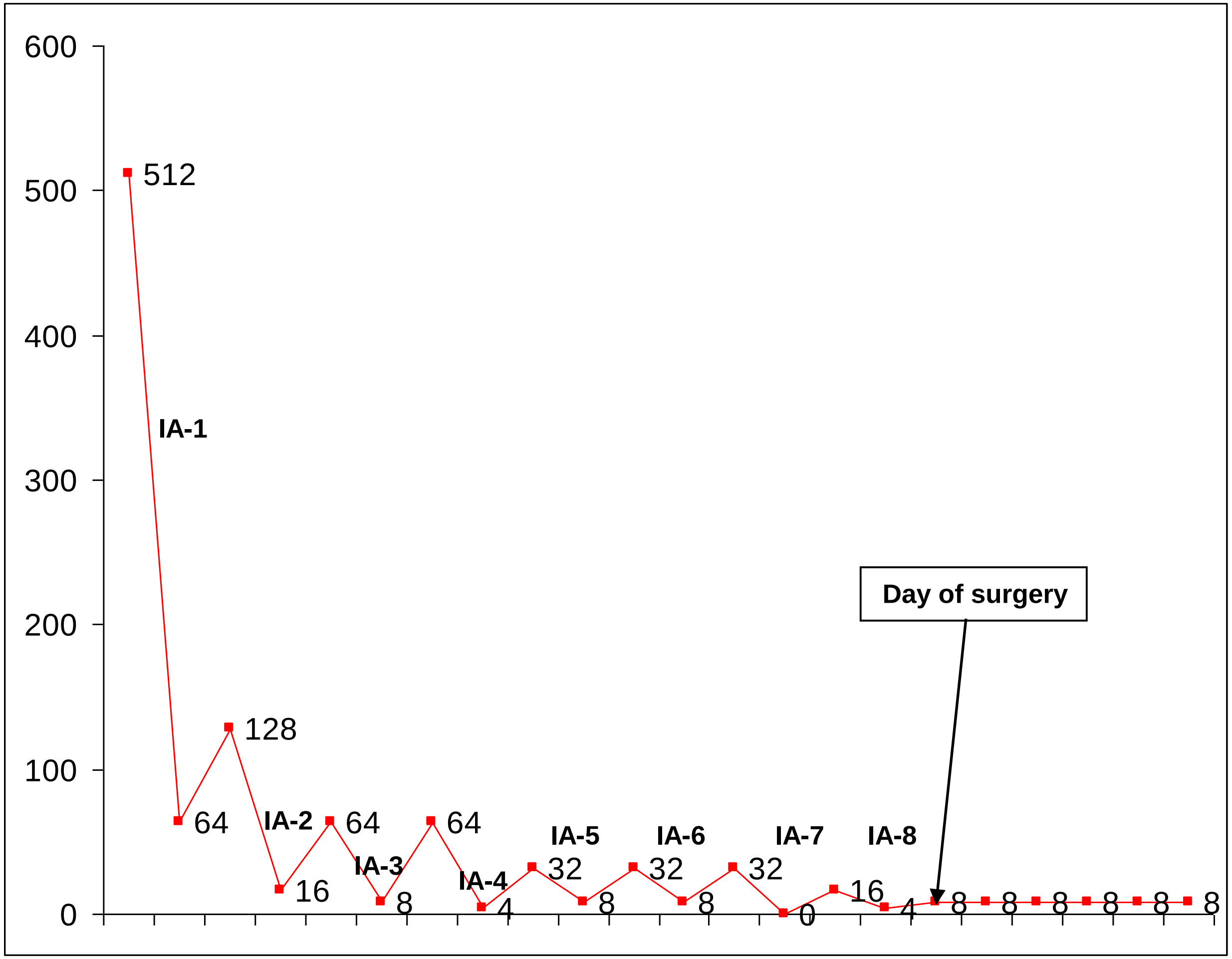
Patient 1

- Potential Recipient
- 56y
- APKD
- CAPD 5y
- Blood Group O

- Potential Donor
- 54y Brother
- HLA compatible
- ABO incompatible
- Blood Group A1

- Paired Scheme
- Several matching runs

- Potential recipient Anti-A titre 1/512


600
500
400
300
200
100
0
512
IA-1
128
64
IA-2
64
64
16
IA-3
8
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32
8
IA-6
32
8
IA-7
32
0
IA-8
16
4
Day of surgery
8
8
8
8
8
8

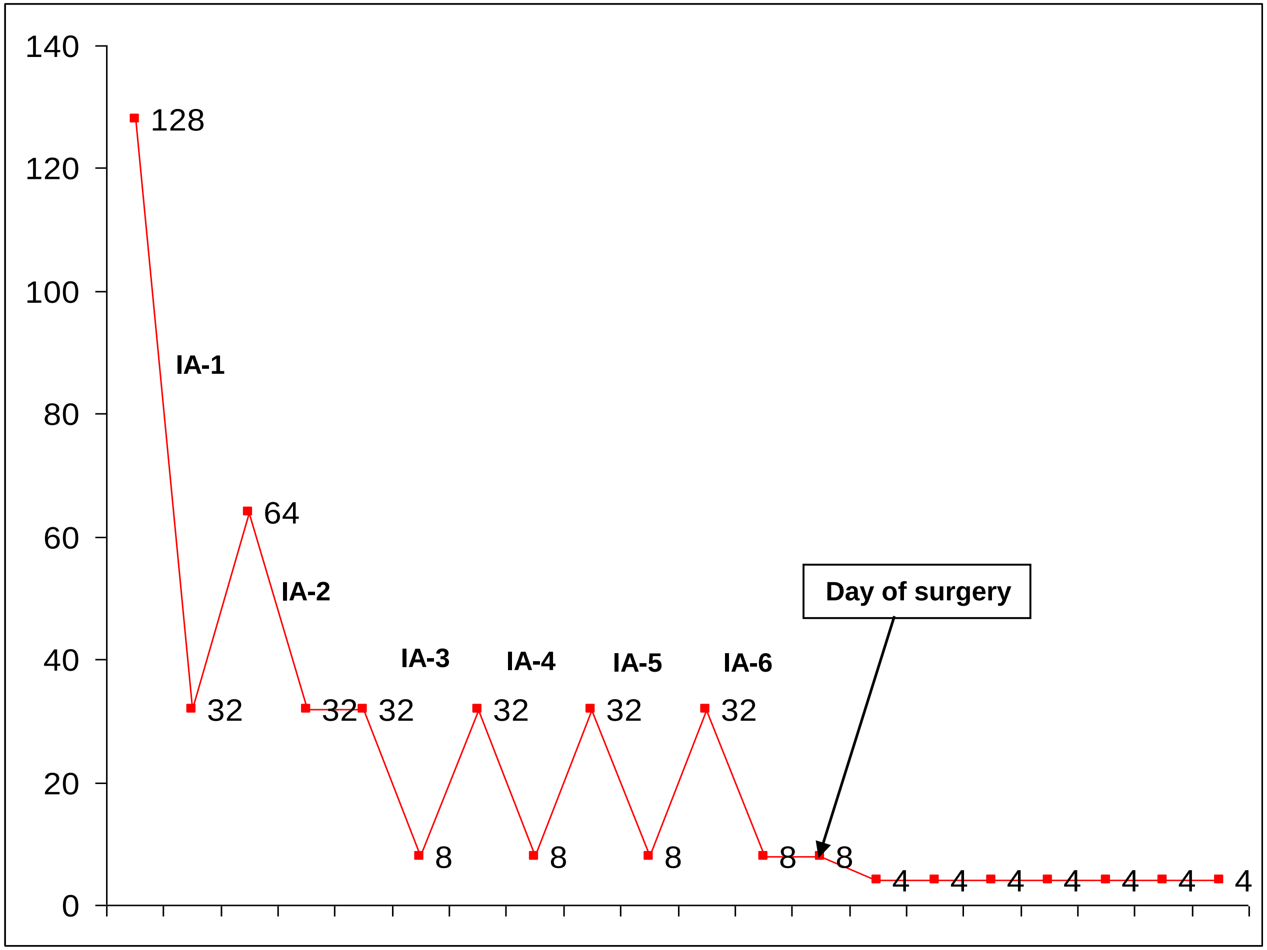
Patient 1

Patient 2

- Potential recipient
- 41y
- IgA Nephropathy
- Maintenance Haemodialysis
- Groin Tesio line access
- Anticoagulated for repeated access thrombosis
- Blood Group B and Highly sensitised

- Potential Donor
- 36y sister
- HLA compatible
- ABO Incompatible
- Blood Group AB

- Predicted match on Paired Scheme ~1%
- Potential recipient initial Anti-A titre 1/512, but lower at the time of treatment



140
120
100
80
60
40
20
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128
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IA-5
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Day of surgery
8
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Patient 2

Plasmapheresis, CMV Hyperimmune Globulin and Anti-CD20 Allow ABO-Incompatible Renal Transplantation Without Splenectomy

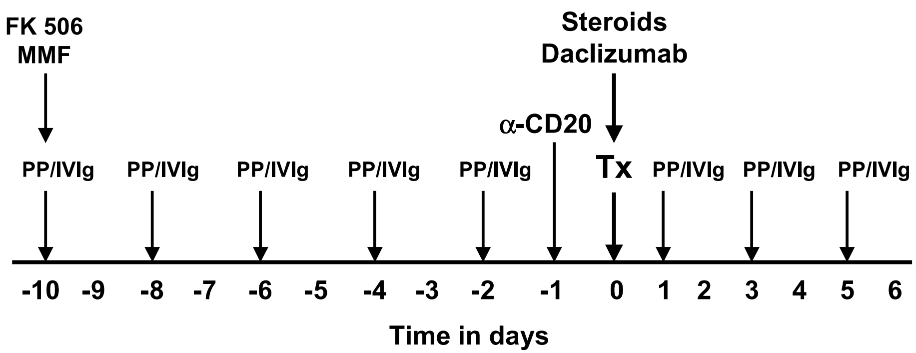


Table 1: Donor and recipient characteristics

n	Donor ABO	Recipient ABO	Recipient age	Recipient gender	Cause of end-stage renal disease	No. PP/CMVIg Pre-tx[a]	No. PP/CMVIg Post-tx[b]	Complications
1	B	O	63	Male	FSGS[c]	5	3	–
2	A_2	O	52	Male	Diabetes mellitus	10[d]	3	Unstable angina[d]
3	A_2	B	73	Male	Chronic glomerulonephritis	2	2	–
4	AB	A	32	Male	Diabetes mellitus	3	3	Acute cellular rejection
5	A_1	O	53	Female	Polycystic kidney disease	5	4	UTI[e], lymphocele
6	B	O	61	Male	FSGS[c]	5	5	Urinary retention, UTI[e]
[f]			58 (32–73)			5 (2–10)	3 (2–5)	

Sonnenday et al. Am J Transplant 2004;4:1315-1322

Plasmapheresis, CMV Hyperimmune Globulin and Anti-CD20 Allow ABO-Incompatible Renal Transplantation Without Splenectomy

Table 2: Isoagglutinin titer and renal allograft function

n	Donor ABO	Recipient ABO	Initial titer	Titer at transplant	Current titer	Current serum Cr (mg/dL)	Current CrCl[a] (mL/min)	Follow-up time (months)
1	B	O	32	2	16	1.6	62	14
2	A_2	O	128[b]	16	32	1.3	113	13
3	A_2	B	8	2	1	1.3	49	13
4	AB	A	32	8	16	1.5	107	11
5	A_1	O	128	8	4	1.1	58	8
6	B	O	128	16	16	1.1	111	4
[c]			80 (8–128)	8 (2–16)	16 (1–32)	1.3 ± 0.1	83.2 ± 12.1	12 (4–14)

Table 3: Histologic evaluation and C4d staining of protocol allograft biopsies

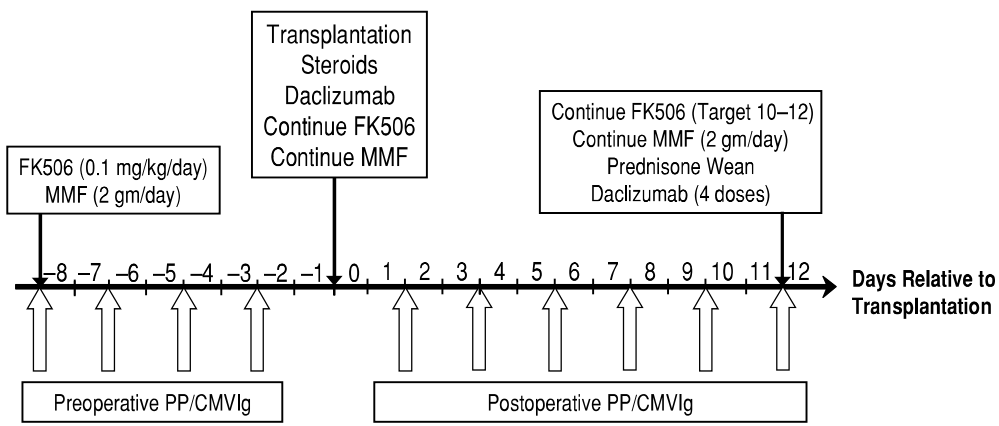
			Post-perfusion			1 month			3 month			6 month			12 months		
n	Donor ABO	Recipient ABO	Acute Banff[a]	C4d[b]	Chronic Banff[d]	Acute Banff[a]	C4d[b]	Chronic Banff[d]	Acute Banff[a]	C4d[b]	Chronic Banff[d]	Acute Banff[a]	C4d[b]	Chronic Banff[d]	Acute Banff[a]	C4d[b]	Chronic Banff[d]
1	B	O	NR	0	ND	NR	1+	0	NR	0	3	NR	0	0	NR	0	1
2	A_2	O	NR	ND	ND	NR	0	ND	NR	1+	0	Bord.[c]	1+	2	ND	ND	ND
3	A_2	B	ND	ND	ND	NR	2+	0	NR	1+	0	NR	1–2+	ND	ND	ND	ND
4	AB	A	NR	ND	1.5	NR	1–2+	2	IIA	2+	2	NR	2–3+	2	ND	ND	ND
5	A_1	O	ND	ND	ND	NR	ND	0	NR	2–3+	0	NR	2+	0	ND	ND	ND
6	B	O	NR	ND	ND	NR	0	0	ND	ND	ND	ND	ND	ND	ND	ND	ND

Sonnenday et al. Am J Transplant 2004;4:1315-1322

ABO Incompatible High-Titer Renal Transplantation without Splenectomy or Anti-CD20 Treatment

Table 1: Clinical characteristics and outcomes

Patient no	1	2	3	4
Recipient age	72	50	42	60
Cause of renal failure	FSGS	Thin BM	NS	HTN
Donor blood type	A2	A1	A1	B
Recipient blood type	O	O	O	A
No of previous Txs	0	0	2	0
Isoagglutinin titer, initial	64	64	128	64
Isoagglutinin titer, at Tx	2	8	16	2
Isoagglutinin titer, current	4	8	4	2
PP/CMVIg # preoperative Rx	4	5*	5	4
PP/CMVIg # postoperative Rx	5	8	7	6
Creatinine, 1 week	0.9	0.8	1.6	0.9
Creatinine, 1 month	1.1	0.9	1.1	0.9
Creatinine, current	**1.2**	**1.0**	**1.2**	**0.9**
Episodes of AMR	0	0	0	0
Episodes of cellular rejection	0	0	1**	0
Follow-up (weeks)	46	29	11	10



Segev et al. Am J Transplant 2005;5:2570-2575

ABO Incompatible Renal Transplantation: A Paradigm Ready for Broad Implementation.

TABLE 2. Demographic characteristics of blood-type incompatible (ABOi) recipients transplanted through the Johns Hopkins Incompatible Kidney Transplant Program between 1999 and 2007

Characteristics	Overall	First era: Splenectomy only	First era: Rituximab only	First era: Splenectomy and rituximab	First era: All treatments[a]	Second era[b]	HLA identical/ABOi	+XM/ABOi[c]
N	60	14	15	3	32	28	6	11
Age[d] (range) (yr)	51 (20–73)	40 (20–60)	54 (27–73)	36 (34–57)	50 (20–73)	51 (20–73)	41 (36–55)	36 (27–69)
Gender (n)								
Male	29	6	8	1	15	14	2	2
Female	31	8	7	2	17	14	4	9
Ethnicity (n)								
White	44	12	10	3	25	19	6	8
Black	12	2	3	0	5	7	0	1
Hispanic	1	0	0	0	0	1	0	0
Other	3	0	2	0	2	1	0	2
Peak PRA								
Median (range)	6 (0–100)	5 (0–100)	0 (0–94)	45 (0–100)	5 (0–100)	7 (0–92)	92 (6–100)	76 (5–100)
Number with PRA >80	15	5	5	1	11	4	4	4
Previous transplants (n)	17	4	5	2	11	6	2	6
Previous pregnancy[e] (n)	10	4	2	1	7	3	3	5
Previous transfusions (n)	15	6	5	1	12	3	3	6
Follow-up[f] (range)	29.1 (0.3–101)	52.8 (0.8–101)	19 (0.3–60.9)	62.8 (43.8–72.2)	42 (0.3–101)	21 (0.4–43.5)	28.8 (1–36.2)	15.9 (0.3–64.4)
Starting AHG titer[g] (range)	128 (4–1024)	128 (16–256)	64 (4–256)	512 (16–1024)	128 (4–1024)	128 (16–512)	128 (128–512)	64 (4–256)
Donor								
A1	32	7	9	3	19	13	6	6
A2	7	2	2	0	4	3	0	1
B	13	1	2	0	3	10	0	2
AB	8	4	2	0	6	2	0	2

Montgomery et al. Transplantation 2009;87:1246-1255

ABO Incompatible Renal Transplantation: A Paradigm Ready for Broad Implementation.

TABLE 3. Summary of isohemagglutinin titers and desensitization treatments required before and after ABOi kidney transplantation

		First era						
Characteristics	Overall	Splenectomy only	Rituximab only	Splenectomy and rituximab	All treatments[a]	Second era[b]	HLA Identical/ABOi	+XM/ABOi[c]
Anti-AHG titer[d]								
Initial	128 (4–1024)	128 (16–256)	64 (4–256)	512 (16–1024)	128 (4–1024)	128 (16–512)	128 (128–512)	64 (4–256)
At transplant	8 (0–16)	8 (2–16)	4 (0–16)	16 (16)	8 (0–16)	8 (2–16)	16 (4–16)	4 (0–16)
Current	8 (1–512)	16 (2–512)	4 (1–16)	8 (1–256)	8 (1–512)	8 (1–64)	8 (2–512)	8 (1–16)
Plasmapheresis[e]								
Pretransplant	6 (2–31)	6 (4–9)	5 (2–31)	12 (8–16)	6 (2–31)	6 (3–10)	6 (6–16)	7 (3–9)
Posttransplant	5 (2–12)	4 (2–6)	5 (2–12)	3 (3–7)	4 (2–12)	5 (2–10)	4 (2–8)	6 (2–12)

In all cases, the isohemagglutinin titers were <16 at the time of transplant.
[a] Includes those patients who had splenectomy or anti-CD20 therapy in preparation for transplant.
[b] Includes those patients desensitized without the addition of splenectomy or anti-CD20 therapy.
[c] ABO incompatible and positive crossmatch.
[d] Median anti-AHG titer (range).
[e] Median number of plasmapheresis treatments (range).
HLA, human leukocyte antigen; ABOi, ABO incompatible; +XM, positive cross match.

TABLE 5. Renal Function among ABOi kidney transplant recipients transplanted at Johns Hopkins Hospital between 1999 and 2007

		First era						
Renal function	Overall	Splenectomy only	Rituximab only	Splenectomy and rituximab	All treatments[a]	Second era[b]	HLA Identical/ABOi	+XM/ABOi[c]
Serum creatinine[d]								
1 yr	1.2 (0.7–3.2)	1.1 (0.9–2)	1.4 (0.9–3.2)	1 (0.9–1.1)	1.3 (0.9–3.2)	1.2 (0.7, 2.1)	1.1 (0.9–1.3)	1 (0.7–1.2)
3 yr	1.2 (0.8–3)	1.1 (0.8–1.7)	1.3 (1.1–3)	1 (0.9–1)	1.2 (0.8–3)	1.3 (1.0–1.7)	–	1.1 (1–1.2)
5 yr	1.3 (0.8–1.8)	1.3 (0.8–1.4)	1.4 (1.2–1.8)	1.1 (0.9–1.2)	1.2 (0.8–1.8)	–	–	–
Current	1.2 (0.7–2.7)	1.2 (0.8–1.7)	1.2 (0.9–1.8)	0.9 (0.8–1.2)	1.3 (0.8–1.8)	1.3 (0.7–2.7)	1.4 (0.8–1.5)	1.1 (0.7–1.6)
Creatinine clearance[e]								
1 yr	60.4 (20.8–92.8)	66.8 (27.1–92.8)	52.4 (20.8–79.4)	73.5 (67.6–75.4)	58.9 (20.8–92.8)	61.2 (30.9–88.3)	75.4 (49.3–76.7)	67.6 (48.1–92.8)
3 yr	61.9 (22.8–113.5)	60.9 (32.7–113.5)	59.2 (22.8–74.8)	80 (67.6–92.6)	62.0 (22.8–113.5)	60.3 (43.6–70)	63.4 (54.7–67.6)	63.4 (54.7–67.6)
5 yr	69.2 (40.6–86.4)	77.8 (69.2–86.4)	40.6	71.4 (66.4–76.3)	69.2 (40.6–86.4)	–	–	76.3
Current	61.2 (32.6–167.5)	59.7 (39.3–86.4)	63 (40.6–96.9)	76.3 (66.4–86.4)	63.2 (39.3–96.9)	60.5 (32.6–167.5)	58.1 (51.5–86.4)	65.1 (39.3–96.9)

Montgomery et al. Transplantation 2009;87:1246-1255

ABO Incompatible Renal Transplantation: A Paradigm Ready for Broad Implementation.

TABLE 6. Incidences of acute rejection episodes among ABO incompatible kidney transplant recipients transplanted at Johns Hopkins Hospital between 1999 and 2007

		First era						
Rejection episodes	**Overall**	**Splenectomy only**	**Rituximab only**	**Splenectomy and rituximab**	**All treatments[a]**	**Second era[b]**	**HLA Identical/ ABOi**	**+XM/ABOi[c]**
Hyperacute	None	None	None	None	None	None	None	None
Clinical acute								
Antibody mediated	11	3	3	0	6	5	2	4
Cellular	11	0	6	2	8	3	1	3
Banff 1A	4	0	1	0	1	3	0	0
Banff 1B	0	0	0	0	0	0	0	0
Banff 2A	3	0	2	1	3	0	1	0
Banff 2B	4	0	3	1	4	0	0	3
Sub-clinical Acute[d]								
Antibody mediated	7	2	1	1	4	3	0	2
Cellular	10	2	2	2	6	4	1	0
Banff 1A	4	0	1	2	3	1	0	0
Banff 1B	3	1	0	0	1	2	0	0
Banff 2A	3	1	1	0	2	1	1	0
Banff 2B	0	0	0	0	0	0	0	0
Chronic[e]								

Montgomery et al. Transplantation 2009;87:1246-1255

ABO incompatible renal transplantation without antibody removal using conventional immunosuppression alone.

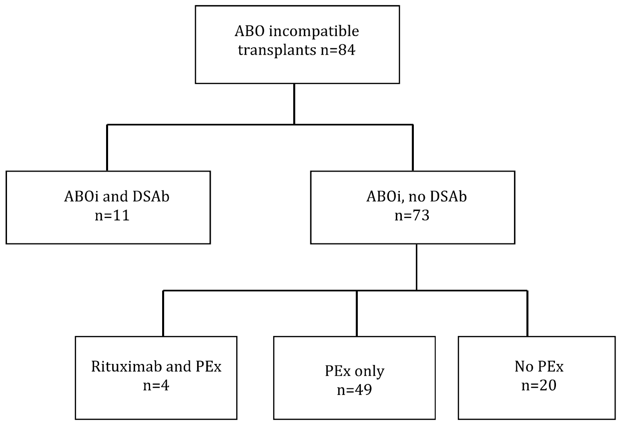


Table 3: Blood group incompatibilities and antibody titers by three methods

Donor blood group	Recipient blood group	Tube titer	Ortho titer	Diamed gel card titer
A1	O	32	16	4
A1	O	64	8	4
A1[c]	B	16	4	2
A2	O	32	4	1
A2	O	8	4	2
A2[b]	O	8	4	2
A2	B	1	1	1
B	O	32	4	2
B	A	128	8	4
B	A	16	2	1
B	A	32	4	4
B	A	32	8	2
B	A	8	4	1
B	A	16	16	4
B	A	1	1	1
B[a]	A	32	16	4
A1B	A	8	2	1
A1B	A	16	8	2
A1B	A	8	2	1
A1B[d]	B	32	8	2

Table 1: Immunosuppression protocol for patients undergoing ABO incompatible transplantation at Royal Melbourne Hospital

	Dosing
Basiliximab	20 mg days 0 and 4
Steroids	Methylprednisolone 500 mg at transplant, then prednisolone 25 mg daily for 4 weeks, tapered to 5 mg daily by week 12
Mycophenolate	500 mg bid commencing 7–10 days pretransplant, increased to 1000 mg bid as tolerated or at time of transplant. Taper to a total dose of 1500 mg/day by weeks 3–6, then 1000 mg/day by weeks 10–12
Tacrolimus	0.05 mg/kg bid commencing 2–3 days pretransplant, adjusted to levels of 9–12 ng/mL for 2 weeks, 8–10 ng/mL weeks 3–4, 5–8 ng/mL weeks 5–24, 3–7 ng/mL weeks 25–52 and 2–4 ng/mL beyond 1 year

Masterson et al. Am Journal of Transplant 2014;14:2807-2813.

Early post-transplant complications following ABO-incompatible transplantation

	ABOi patients (n=44)	ABOc patients (n=44)	P value
Overall bleeding complications (n, %)	20 (40.4)	8 (18.2)	0.006
Renal-artery anastomosis leakage (n; %)	2 (4.5)	0	NS
Intraoperative bleeding (n; %)	12 (27.3)	2 (4.5)	0.0004
Large wound hematomas (n; %)	16 (36.3)	6 (13.6)	0.013
Gross hematuria after postoperative D5 (n; %)	3 (6.8)	2 (4.5)	NS
No. of patients requiring red-blood cell transfusions between D0 and D10 (n; %)	35 (79.5)	12 (27.3)	0.00002
Intraoperative BT (n; %)	14 (31.8)	3 (6.8)	0.006
D0 BT excluding intraoperative (n; %)	12 (27.3)	3 (6.8)	0.023
D1 BT (n; %)	10 (22.7)	4 (9.1)	NS
Number of BTs/patient	3.5 ± 3.4	0.8 ± 1.9	0.00002
D0 (pre-op) fibrinogen (g/L)	1.88 ± 0.62	3.65 ± 1.62	0.0006
D0 platelets (pre-op/mm^3)	146520 ± 35880	195610 ± 50940	0.00001
D0 (pre-op) prothrombin time (%)	83.8 ± 12.1	89.8 ± 9.5	0.012
D0 (pre-op)activated cephalin time(s)	27.1 ± 4.1	29.5 ± 4	0.005
D0 Hb (pre-op) (g/dL)	10.1 ± 1.2	10.9 ± 1.5	0.006

Abbreviations: D, day; BT, blood transfusion, i.e., red blood-cell packs; Hb, hemoglobin; ABOi, ABO-incompatible; ABOc, ABO-compatible.

Bleeding complications and requirements for a blood transfusion

J Nephropathol 2016 5(1):19-27. Bennani et al

Early post-transplant complications following ABO-incompatible transplantation

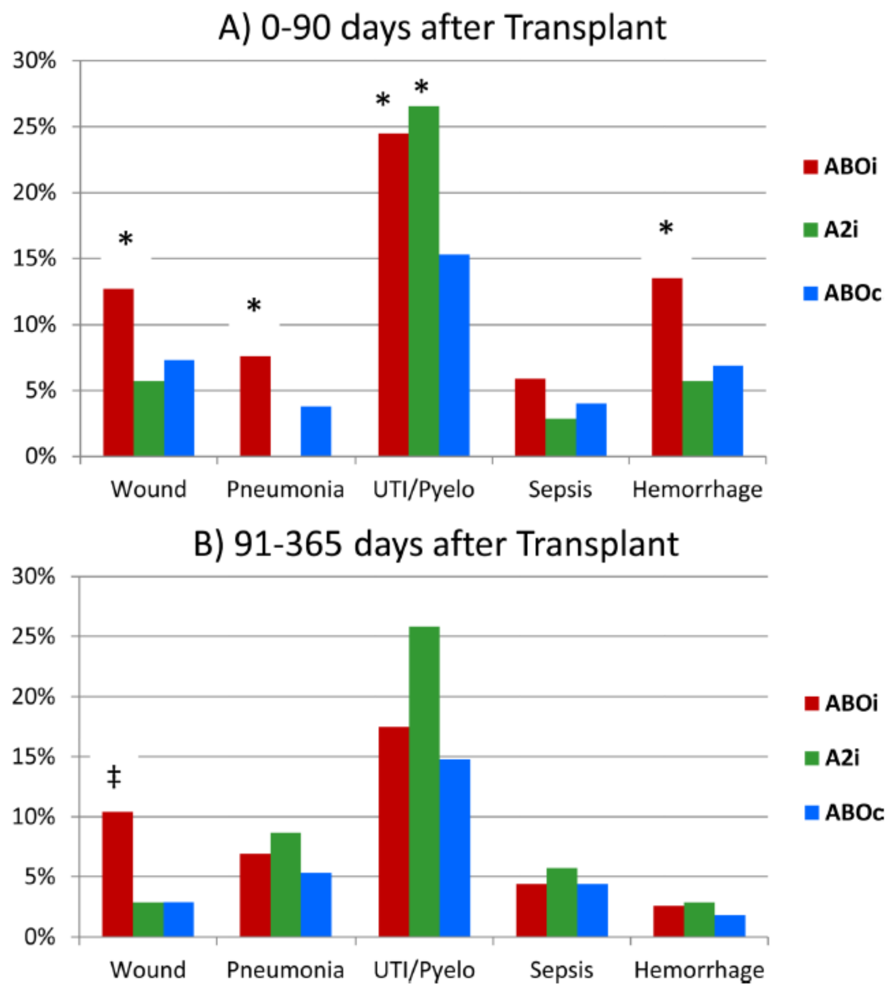
	ABOi patients (n=44)	ABOc patients (n=44)	P value
Renal artery thrombosis (n)	0	0	NS
Renal venous thrombosis (n)	1	0	NS
Renal artery stenosis (n; %)	4 (9.1)	6 (13.6)	NS
Urinary leakage (n; %)	0	2 (4.5)	NS
Lymphoceles (n; %)	8 (18.2)	7 (16)	NS
Wound dehiscence (n; %), requiring surgery (n)	5 (11.3), 3	2 (4.5), 1	NS
Peritoneal breach (n; %)	1 (2.3)	0	NS

Abbreviations: ABOi, ABO-incompatible; ABOc, ABO-compatible.

Post-transplant surgical complications

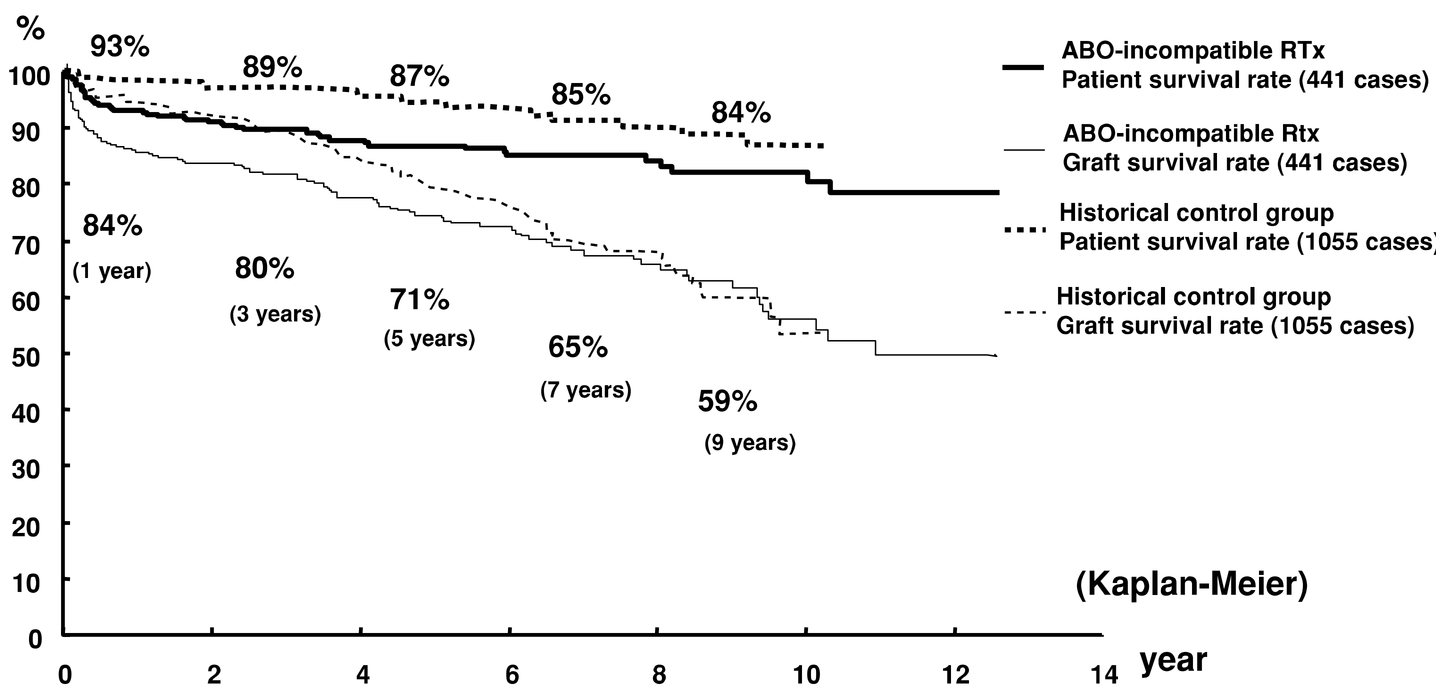
J Nephropathol 2016 5(1):19-27. Bennani et al

Early clinical complications after ABO incompatible live donor kidney transplantation



Early clinical complications after ABO incompatible live donor kidney transplantation:A national study of Medicare-insured recipients. Lentine et al Transplantation. 2014 July 15; 98(1): 54–65.

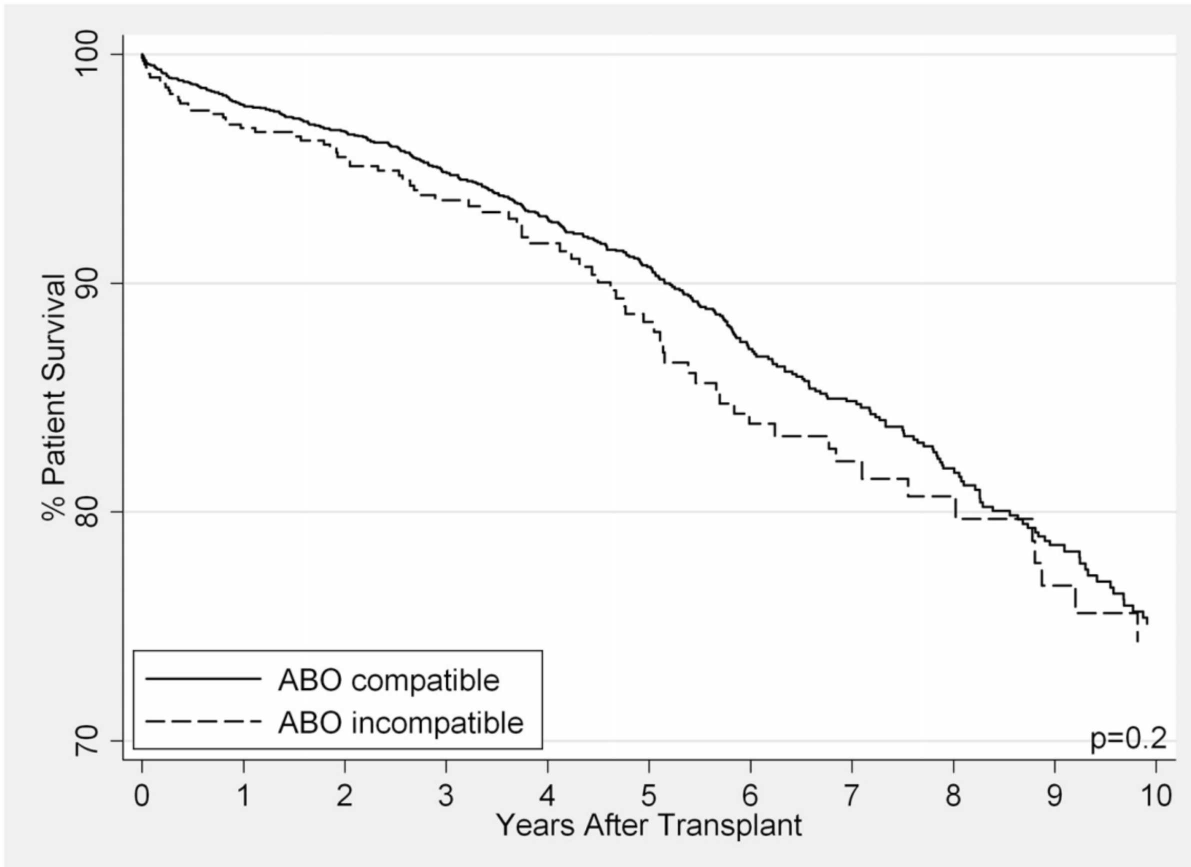
Excellent Long-term Outcome of ABO-Incompatible Living Donor Kidney Transplantation in Japan



1989-2001 441 transplants carried out

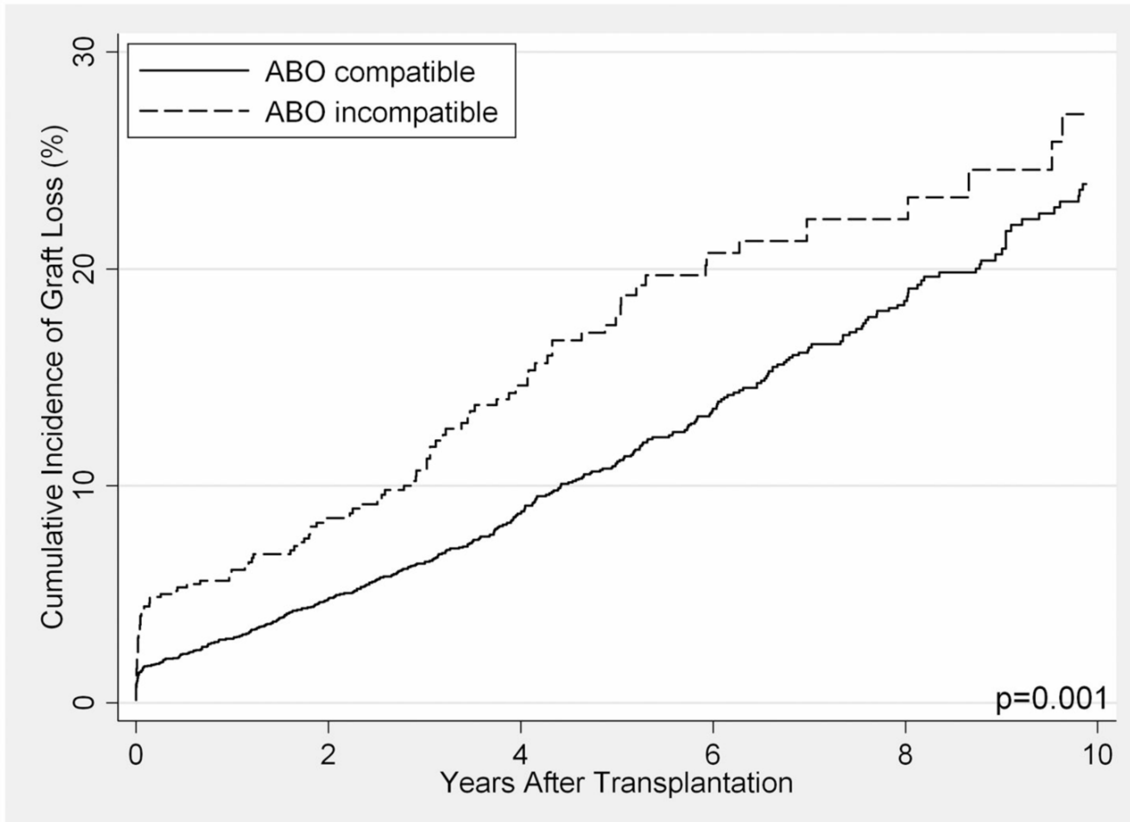
Takahashi et al. Am J Transplant 2004;4:1089-1096

Outcomes of ABO Incompatible Kidney Transplantation - USA



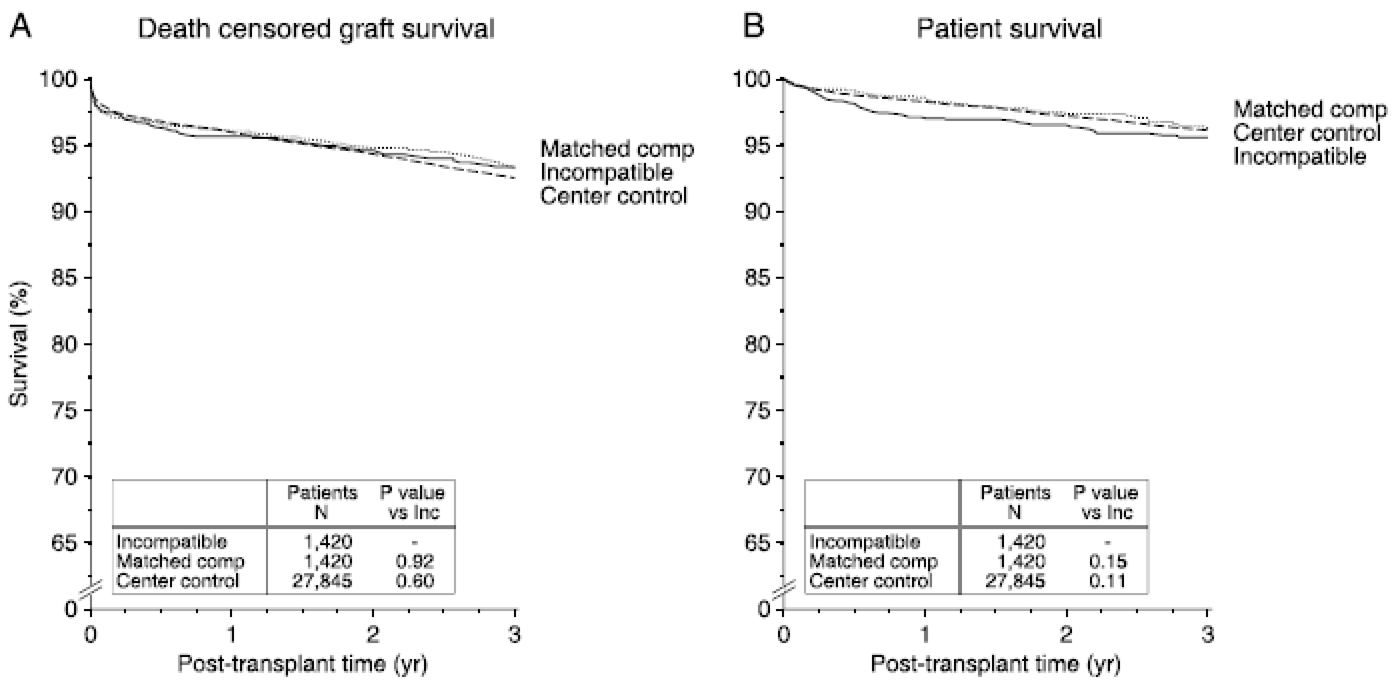
Outcomes of ABO-Incompatible Kidney Transplantation in the United States. Montgomery et al. Transplantation. 2012 March 27; 93(6): 603–609.

Outcomes of ABO Incompatible Kidney Transplantation - USA



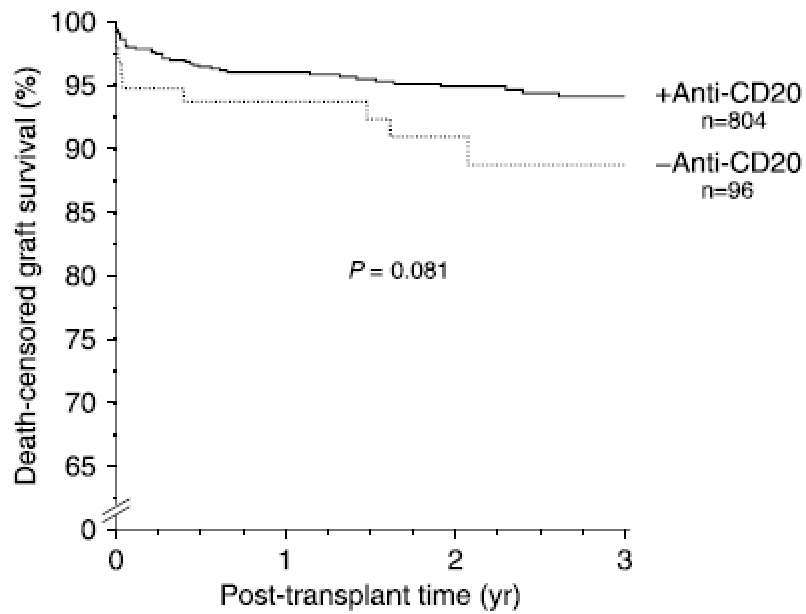
Outcomes of ABO-Incompatible Kidney Transplantation in the United States. Montgomery et al. Transplantation. 2012 March 27; 93(6): 603–609.

Outcomes of ABO Incompatible Kidney Transplantation - Europe



Three-Year Outcomes Following 1420 ABO-incompatible Living-Donor Kidney Transplants Performed After ABO Antibody Reduction:Results from 101 Centers. Opelz et al . Transplantation 2015:99;400-404

Outcomes of ABO Incompatible Kidney Transplantation - Europe



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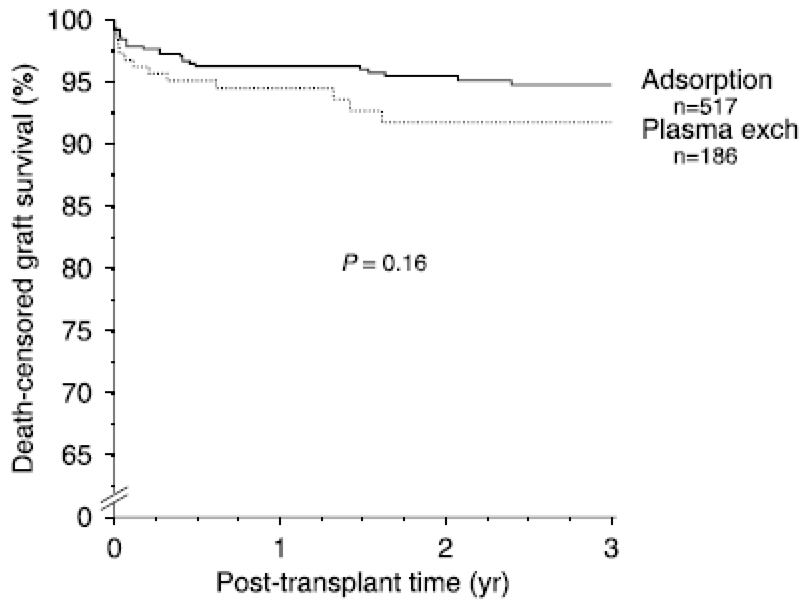
Outcomes of ABO Incompatible Kidney Transplantation - Europe



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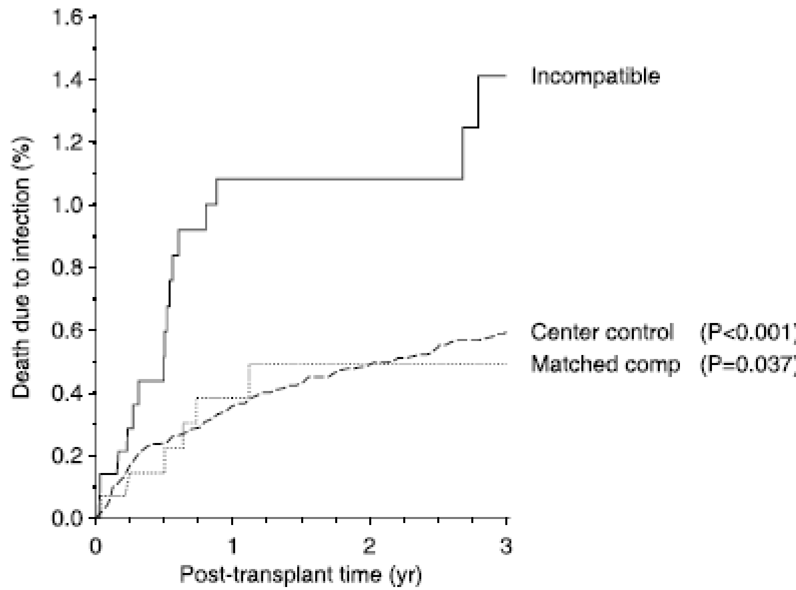
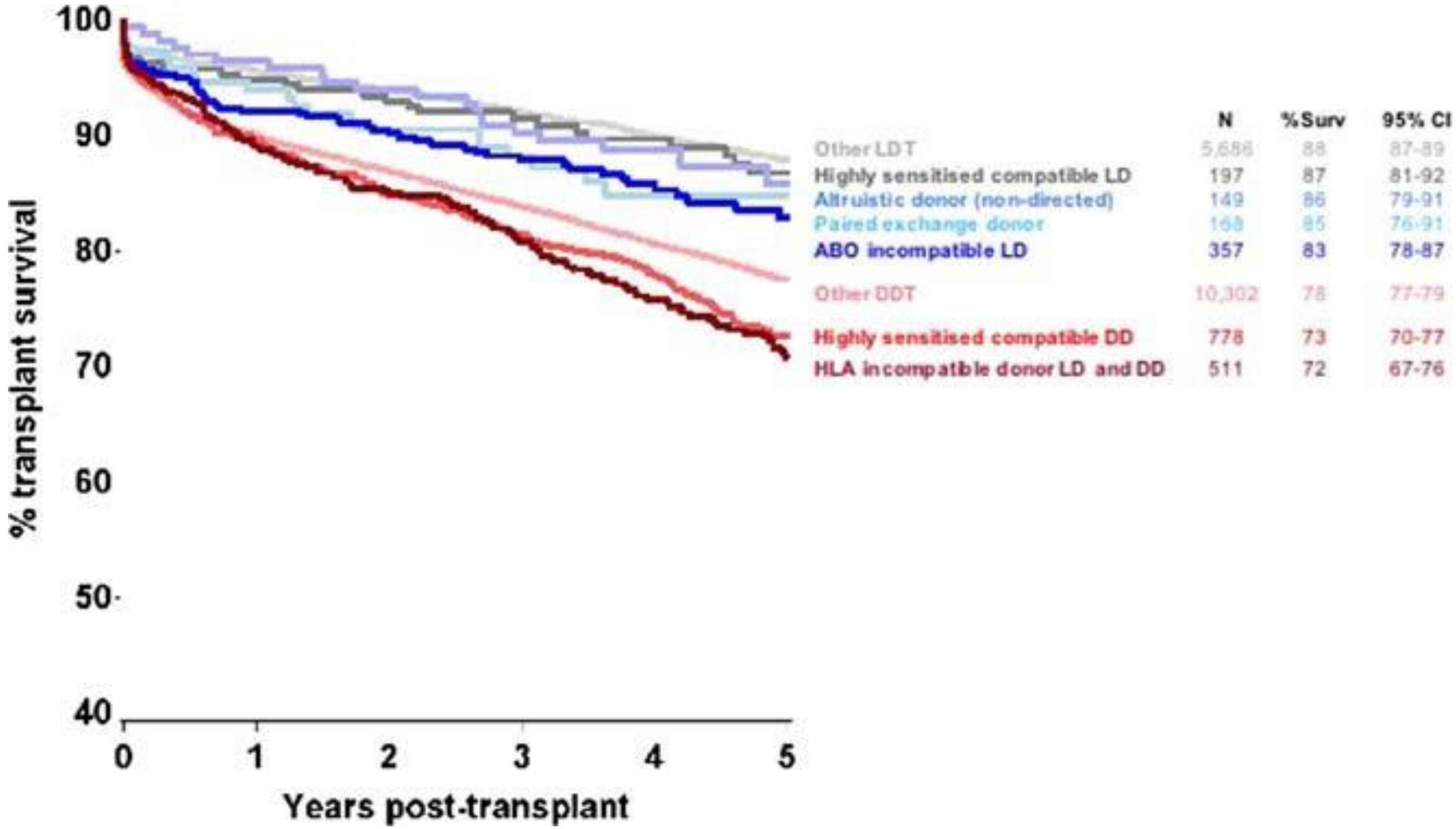
Outcomes of ABO Incompatible Kidney Transplantation - Europe



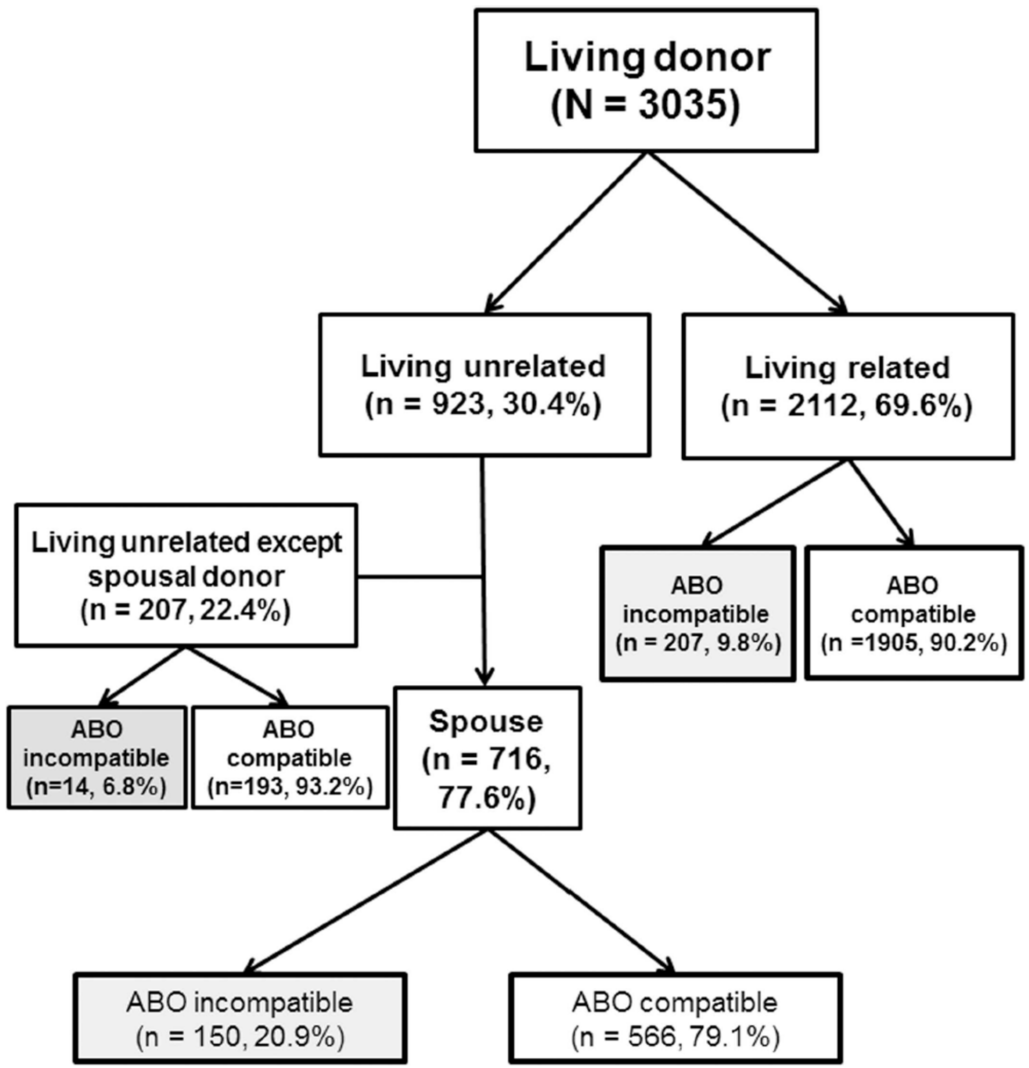
Three-Year Outcomes Following 1420 ABO-incompatible Living-Donor Kidney Transplants Performed After ABO Antibody Reduction:Results from 101 Centers. Opelz et al . Transplantation 2015:99;400-404

The UK National Registry of ABO and HLA Antibody Incompatible Renal Transplantation: Pretransplant Factors Associated With Outcome in 879 Transplants



Five-year transplant survival for all kidney only transplants in the United Kingdom between January 1, 2005, and December 31, 2012. Transplantation Direct 2017;3: e181; doi: 10.1097/TXD.0000000000000695. Published online 26 June, 2017. Laura Pankhurst et al

Enabling spousal donation – the South Korean experience



Impact of ABO incompatible kidney transplantation on living donor transplantation Yu et al 2017. PLoS ONE 12(3):e0173878

ABOi economics

- USA 2000-2011
- 271 ABOi (Patient survival 88% /Graft survival 76% at 3 years)
- 26,504 ABOc transplants (Patient survival 93% /Graft survival 85% at 3 years)

- $65,000 ABOi
- $32,000 ABOc
- ABOi more expensive over the initial 3 years

- *[Much lower additional costs in Europe for ABOi]*

- 1 years Medicare Haemodialysis cost in USA $87,500 - with an average waiting time of 4.5 years ($390,000)

- No difference in outcomes between low and high volume centres

Economic impacts of ABO incompatible live donor kidney transplantation: A national study of Medicare-insured recipients. Axelrod et al Am J Transplant. 2016 ;16(5): 1465–1473.

ABO incompatible transplantation

- ABO incompatible transplantation
  - excellent outcomes
  - different protocols with similar outcomes
  - the increased bleeding and infection risk is important to recognise
  - for some recipients an ABOi transplant is the best treatment

Present Experiences in a Series of 26 ABO-Incompatible Living Donor Renal Allografts

G.P.J. Alexandre, J.P. Squifflet, M. De Bruyère, D. Latinne, R. Reding, P. Gianello, M. Carlier, and Y. Pirson

Meanwhile, it is of utmost importance to precisely clarify the conditions of success in ABO-incompatible organ grafts now possible for a group of patients who before were denied the benefit of such a transplant.

Transplantation Proceedings, Vol XIX, No 6 (December), 1987:. pp 4538-4542