

SUPPLEMENTARY APPENDIX

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Supplementary Table 1. Multivariable dynamic antibody-mediated rejection prediction Cox model with change in peritubular Banff score after treatment coded as a categorical variable

	Number of patients	Number of events	HR	95%CI	P
eGFR at ABMR diagnosis (per 1-mL/min/1.73 m ² increment)	278	60	0.93	[0.91-0.95]	<0.001
Interstitial fibrosis/Tubular atrophy at ABMR diagnosis					
Banff score 0	130	16	1		
Banff score >0	148	44	2.49	[1.39-4.47]	0.002
eGFR relative change after treatment (log ₁₀ [value+0.7], continuous)	278	60	0.23	[0.16-0.34]	<0.001
ΔPeritubular capillaritis Banff score after treatment					
ΔBanff score <0	158	25	1		
ΔBanff score ≥0	120	35	1.67	[1.00-2.82]	0.052
Anti-HLA DSA MFI relative change after treatment (continuous)	278	60	1.32	[1.13-1.54]	<0.001

ABMR, antibody-mediated rejection; DSA, donor-specific antibody; HLA, human leucocyte antigen; MFI, mean fluorescence intensity

$$\text{Relative change} = \frac{\text{value after treatment} - \text{value at ABMR diagnosis}}{\text{value at ABMR diagnosis}}$$

Δ = value after treatment – value at ABMR diagnosis

Supplementary Table 2. Characteristics of the external validation cohort at the time of transplantation

Recipient characteristics	N	
Age (years) - mean±SD	202	47.6±14.6
Male gender (male) - n (%)	202	119 (58.9)
Retransplantation - n (%)	202	34 (16.8)
Preemptive transplantation - n (%)	202	21 (10.4)
Time since dialysis (years) - mean±SD	181	3.9±3.0
Blood type - n (%)	202	
A		83 (41.1)
B		28 (13.9)
O		85 (42.1)
AB		6 (3.0)
Chronic kidney disease - n (%)	202	
Glomerulopathy		60 (29.7)
Vascular nephropathy		17 (8.4)
Chronic interstitial nephropathy		22 (10.9)
Malformative uropathy		10 (5.0)
Polycystic kidney disease		12 (5.9)
Diabetes		18 (8.9)
Other		13 (6.4)
Not determined		50 (24.8)
Donor characteristics		
Age (years) - mean±SD	202	51.4±17.0
Male sex - n (%)	202	107 (53.0)
Type - n (%)	202	
Living		32 (15.8)
Cerebrovascular death		64 (31.7)
Other cause of death		104 (52.5)
Terminal serum creatinine (µmol/L) - mean±SD	202	91.1±52.9
Transplant characteristics		
Cold ischemia time (hours) - mean±SD	202	15.8±9
HLA mismatch - mean±SD	202	
A		1.1±0.7
B		1.1±0.7
DR		1.1±0.6
Anti-HLA DSA at the time of transplantation - n (%)	202	63 (31.2)

DSA, donor-specific antibody; HLA, human leukocyte antigen

Supplementary Table 3. Clinical, pathological and immunological characteristics of the external validation cohort at antibody-mediated rejection diagnosis and at the post-treatment evaluation

	N	ABMR diagnosis	Post-treatment	P
Clinical characteristics				
GFR (mL/min/1.73 m ²) - mean±SD	202	35.4±18.9	41.3±18.9	<0.001
Proteinuria (g/g) - mean±SD	202	0.87±1.19	0.78±1.40	0.02
Histological characteristics (Banff scores)				
Glomerulitis - mean±SD	201	1.9±0.9	1.2±1.0	<0.001
Peritubular capillaritis - mean±SD	201	2.0±0.8	1.2±1.0	<0.001
Interstitial inflammation - mean±SD	201	0.6±1.0	0.3±0.6	<0.001
Tubulitis - mean±SD	201	0.7±1.0	0.4±0.8	<0.001
Endarteritis - mean±SD	196	0.4±0.8	0.1±0.4	<0.001
Chronic allograft glomerulopathy - mean±SD	201	0.3±0.8	0.4±0.9	0.006
Interstitial fibrosis/tubular atrophy - mean±SD	201	1.0±1.1	1.4±1.1	<0.001
Arteriosclerosis - mean±SD	196	1.2±1.0	1.4±1.0	0.008
C4d deposition - n (%)	201	119 (59.2)	77 (38.3)	<0.001
Immunodominant anti-HLA DSA characteristics				
MFI - mean±SE	201	4934.1±355.8	2812.8±324.0	<0.001

ABMR, antibody-mediated rejection; DSA, donor-specific antibody; HLA, human leucocyte antigen; GFR, glomerular filtration rate; MFI, mean fluorescence intensity

Supplementary Table 4. Net benefit for adding a new intervention in all kidney transplant recipients with antibody-mediated rejection or according to the antibody-mediated rejection prognostic score

The clinical decision considered here is to add a new intervention to the standard treatment of antibody-mediated rejection. The net benefit for adding a new intervention in all patients with antibody-mediated rejection or according to the antibody-mediated rejection prognostic score is provided for different decision risk thresholds for 6-year allograft loss. The reduction in avoidable interventions per 100 antibody-mediated rejection patients is net of false negatives; i.e., without a decrease in the number of high-risk patients who duly undergo the intervention.

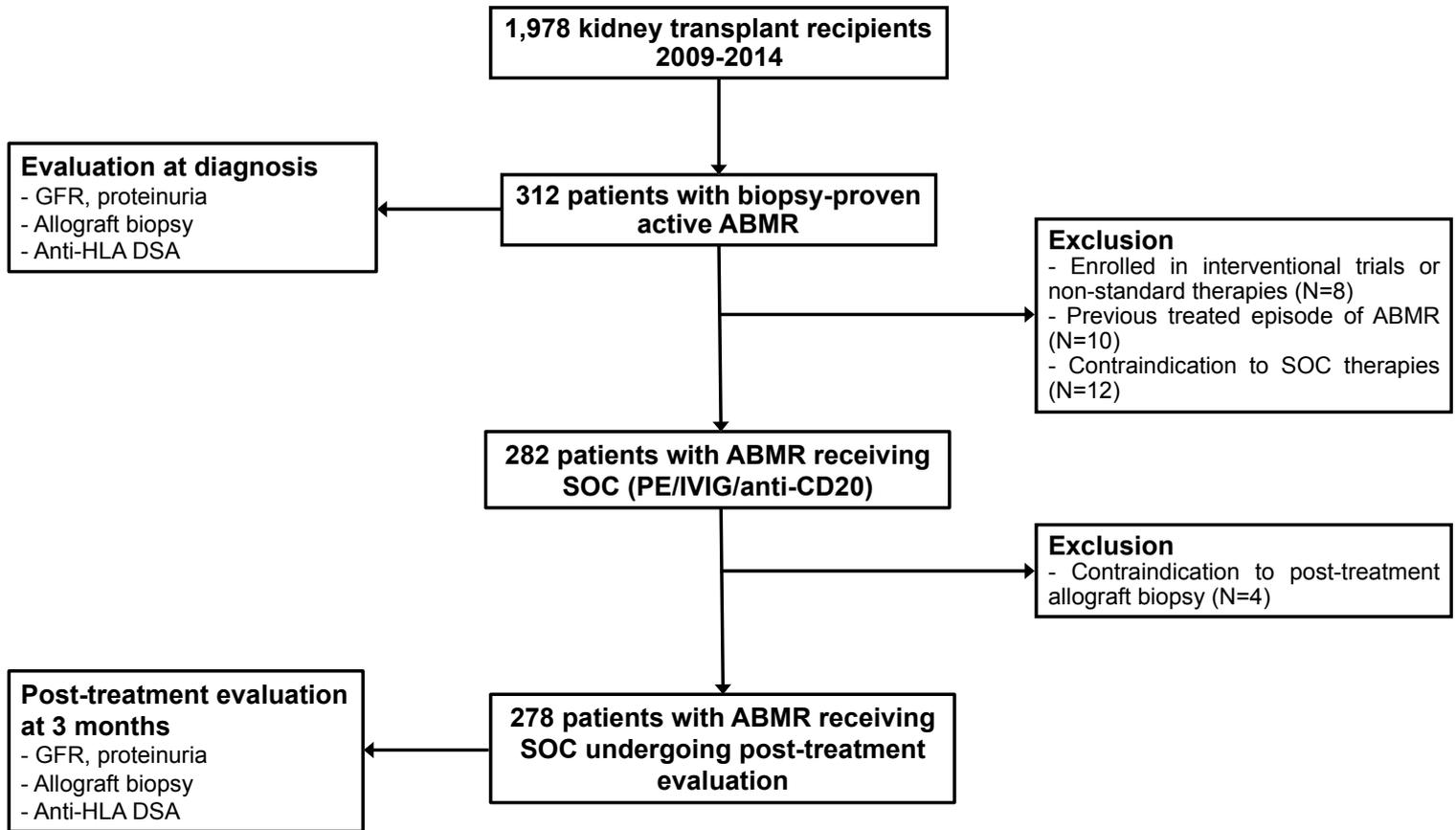
Risk threshold for decision making (6-year allograft loss)	Net benefit		Reduction in avoidable interventions per 100 ABMR patients
	Intervention in all	ABMR prognostic score	
1%	0.208	0.209	10
10%	0.129	0.146	15
20%	0.020	0.110	36
30%	-0.120	0.082	51
40%	-0.307	0.060	55
50%	-0.568	0.058	63
60%	-0.960	0.049	67
70%	-1.614	0.054	71
80%	-2.921	0.04	74
90%	-6.842	0.011	76
99%	-77.420	0	78

ABMR, antibody-mediated rejection

$$\text{Net benefit} = \frac{\text{True Positive Count}}{n} - \frac{\text{False Positive Count}}{n} \left(\frac{p}{1-p} \right)$$

Supplementary Figure 1. Flow diagram of the study population

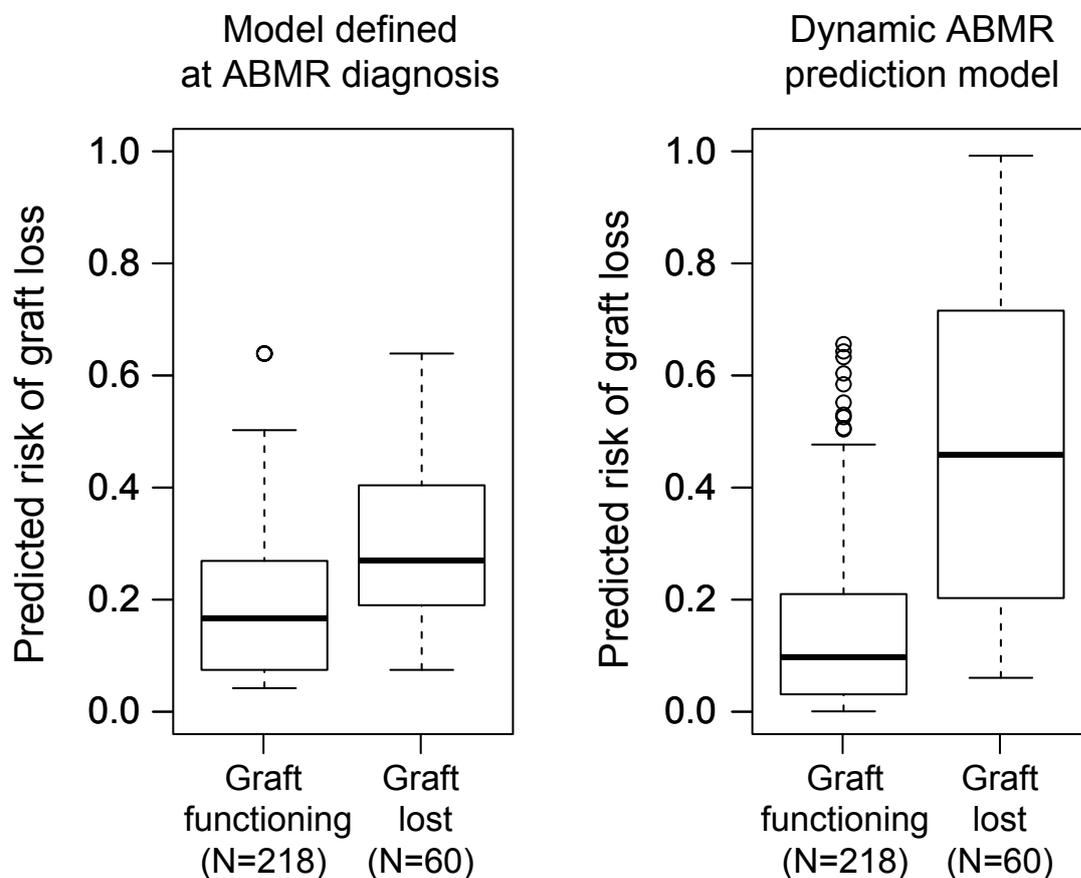
ABMR, antibody-mediated rejection; DSA, donor-specific antibody; GFR, glomerular filtration rate; HLA, human leucocyte antigen; IVIG, intravenous immune globulin; PE, plasma exchange; SOC, standard of care



Supplementary Figure 2. Improvement in the prediction of the risk of kidney allograft loss provided by the dynamic antibody-mediated rejection prediction model including the post-treatment evaluation compared with the prediction made at the time of antibody-mediated rejection diagnosis

The multivariable model for kidney allograft loss defined at the diagnosis of antibody-mediated rejection included glomerular filtration rate, presence of chronic allograft glomerulopathy, presence of interstitial fibrosis and tubular atrophy, and anti-HLA DSA *de novo* status. The multivariable dynamic antibody-mediated rejection prediction model for kidney allograft loss included glomerular filtration rate at diagnosis, presence of interstitial fibrosis and tubular atrophy at diagnosis, change in glomerular filtration rate after treatment, change in peritubular capillaritis Banff score after treatment and change in immunodominant donor-specific anti-HLA antibody mean fluorescence intensity after treatment.

ABMR, antibody-mediated rejection



SUPPLEMENTARY METHODS

Equation of the prognostic score for kidney allograft survival in patients with antibody-mediated rejection

eGFR, estimated glomerular filtration rate; MFI, mean fluorescence intensity of the immunodominant donor-specific anti-HLA antibody

Prognostic score

$$\begin{aligned} &= 0.0765323 \times \text{eGFR}_{\text{diagnosis}} \\ &+ 0.8913344 \times \text{Interstitial fibrosis and tubular atrophy}_{\text{diagnosis}} \begin{pmatrix} 0 \\ 1 \end{pmatrix} \\ &- 1.440734 \times \ln \left(\frac{\text{eGFR}_{\text{post-treatment}} - \text{eGFR}_{\text{diagnosis}}}{\text{eGFR}_{\text{diagnosis}}} + 0.7 \right) \\ &+ 0.4034607 \times (\text{ptc Banff score}_{\text{post-treatment}} - \text{ptc Banff score}_{\text{diagnosis}}) \\ &+ 0.2608125 \times \left(\frac{\text{MFI}_{\text{post-treatment}} - \text{MFI}_{\text{diagnosis}}}{\text{MFI}_{\text{diagnosis}}} \right) \end{aligned}$$