SUPPLEMENTARY TABLES AND FIGURES

Supplementary Table 1: Clinical and histological characteristics according to the antibody-mediated injury phenotypes.

Supplementary Table 2: Clinical and histological characteristics according to the IgG3 status and stratified by the IgG4 status in the recipients with antibody-mediated injury.

Supplementary Table 3: Clinical and histological characteristics according to the IgG4 status and stratified by the IgG3 status in the recipients with antibody-mediated injury.

Supplementary Table 4: Clinical and histological characteristics according to the IgG1 status in the recipients with antibody-mediated injury.

Supplementary Table 5: Clinical and histological characteristics according to the IgG2 status in the recipients with antibody-mediated injury.

Supplementary Table 6: IgG subclass distribution according to the preformed/*de novo* status of the immunodominant donor-specific anti-HLA antibody.

Supplementary Figure 1: Distribution of the immunological variables (MFI level, HLA class specificity, C1q-binding ability and IgG1-4 status) related to the dominant donor-specific anti-HLA antibody in the overall study population.

Supplementary Table 1. Clinical and histological characteristics according to the antibody-mediated injury phenotypes.

	aABMR N=51	sABMR N=36	ABMR-free N=38	p-value
Clinical characteristics				
Time to diagnosis* (d) - median (Q1-Q3)	25 (14 - 52)	366 (361 - 372)	-	-
Baseline eGFR (mL/min/1.73 m^2) - mean ± SD	57.9 ± 17.5	49.5 ± 16.5	57.7 ± 19.1	0.07
eGFR at biopsy (mL/min/1.73 m^2) - mean ± SD	24.5 ± 12.7	49.2 ± 16.2	57.5 ± 19.6	<0.001
Proteinuria at biopsy (g/g) - mean ± SD	1.4 ± 2.0	0.5 ± 1.2	0.2 ± 0.1	0.002
1-year eGFR (mL/min/1.73 m2) - mean ± SD	37.6 ± 17.5	49.2 ± 16.2	57.5 ± 19.6	<0.001
1-year proteinuria (g/g) - mean ± SD	0.8 ± 1.3	0.5 ± 1.2	0.2 ± 0.1	<0.001
Time to failure (d) - median (Q1-Q3)	769 (548 - 1033)	1655 (1151 - 1673)	1650 (-)	-
Histological characteristics (Banff scores)				
g + ptc score - mean ± SD	3.8 ± 1.2	2.8 ± 1.1	0.2 ± 0.5	<0.001
i + t score - mean ± SD	1.5 ± 1.7	0.8 ± 1.1	0.2 ± 0.7	<0.001
v score - mean ± SD	0.6 ± 1.0	0.1 ± 0.5	0	0.03
cg score - mean ± SD	0.2 ± 0.6	0.6 ± 0.8	0	<0.001
IF/TA score - mean ± SD	0.6 ± 0.9	1.7 ± 1.0	0.8 ± 0.9	<0.001
cv score - mean ± SD	1.1 ± 1.0	1.8 ± 0.9	1.0 ± 0.9	0.002
C4d deposition - n (%)	37 (72.6)	10 (27.8)	3 (7.9)	<0.001

aABMR, acute antibody-mediated rejection; cg, allograft glomerulopathy; cv, vascular fibrous intimal thickening; eGFR, estimated glomerular filtration rate; g, glomerulitis; i, mononuclear cell interstitial inflammation; IF/TA, interstitial fibrosis/tubular atrophy; ptc, peritubular capillaritis; sABMR, sub-clinical antibody-mediated rejection; t, tubulitis; v, intimal arteritis

*Time between transplantation and allograft biopsy with concomitant anti-HLA antibodies assessment

Supplementary Table 2. Clinical and histological characteristics according to the IgG3 status and stratified by the IgG4 status in the recipients with antibody-mediated injury.

	IgG4 positive			IgG4 negative		
	IgG3 positive N=9	IgG3 negative N=24	p-value	IgG3 positive N=26	IgG3 negative N=28	p-value
Clinical characteristics						
Time to diagnosis* (d) - median (Q1-Q3)	158 (37-364)	366 (357-372)	0.04	26 (14-52)	65 (17-360)	0.04
eGFR at biopsy (mL/min/1.73 m^2) - mean ± SD	38.2 ± 13.3	49.9 ± 20.1	0.09	25.3 ± 12.7	29.4 ± 15.7	NS
Time to failure (d) - median (Q1-Q3)	377	1666 (1621-1673)	-	650 (474-785)	1353 (1115-1692)	<0.001
Histological characteristics (Banff scores)						
g + ptc score - mean ± SD	3.8 ± 1.4	3.0 ± 1.1	0.12	3.9 ± 1.3	3.1 ± 1.0	0.01
i + t score - mean ± SD	1.2 ± 1.6	0.8 ± 1.2	NS	1.6 ± 1.8	1.1 ± 1.3	NS
v score - mean ± SD	0.1 ± 0.3	0.2 ± 0.7	NS	0.6 ± 0.2	0.5 ± 0.2	NS
cg score - mean ± SD	0.9 ± 1.3	0.7 ± 0.7	NS	0.2 ± 0.6	0.1 ± 0.3	NS
IF/TA score - mean ± SD	1.3 ± 1.0	1.6 ± 0.9	NS	0.4 ± 0.8	1.0 ± 1.2	0.04
cv score - mean ± SD	1.7 ± 1.0	1.7 ± 0.9	NS	1.1 ± 1.0	1.4 ± 1.1	NS
C4d deposition - n (%)	7 (77.8)	4 (16.7)	0.002	21 (80.8)	15 (53.6)	0.03

cg, allograft glomerulopathy; cv, vascular fibrous intimal thickening; eGFR, estimated glomerular filtration rate; g, glomerulitis; i, mononuclear cell interstitial inflammation; IF/TA, interstitial fibrosis/tubular atrophy; ptc, peritubular capillaritis; t, tubulitis; v, intimal arteritis

*Time between transplantation and allograft biopsy with concomitant anti-HLA antibodies assessment

Supplementary Table 3. Clinical and histological characteristics according to the IgG4 status and stratified by the IgG3 status in the recipients with antibody-mediated injury.

	IgG3 positive			IgG3 negative		
	IgG4 positive N=9	IgG4 negative N=26	p-value	IgG4 positive N=24	IgG4 negative N=28	p-value
Clinical characteristics						
Time to diagnosis* (d) - median (Q1-Q3)	158 (37-364)	26 (14-52)	0.003	366 (357-372)	65 (17-360)	<0.001
eGFR at biopsy (mL/min/1.73 m^2) - mean ± SD	38.2 ± 13.3	25.3 ± 12.7	0.03	49.9 ± 20.1	29.4 ± 15.7	<0.001
Time to failure (d) - median (Q1-Q3)	377	650 (174-785)	-	1666 (1621-1673)	1353 (1115-1692)	NS
Histological characteristics (Banff scores)						
g + ptc score - mean ± SD	3.8 ± 1.4	3.9 ± 1.3	NS	3.0 ± 1.1	3.1 ± 1.0	NS
i + t score - mean ± SD	1.2 ± 1.6	1.6 ± 1.8	NS	0.8 ± 1.2	1.1 ± 1.3	NS
v score - mean ± SD	0.1 ± 0.3	0.6 ± 0.9	NS	0.2 ± 0.7	0.5 ± 1.0	NS
cg score - mean ± SD	0.9 ± 1.3	0.2 ± 0.6	0.03	0.7 ± 0.7	0.1 ± 0.3	<0.001
IF/TA score - mean ± SD	1.3 ± 1.0	0.4 ± 0.8	0.004	1.6 ± 0.9	1.0 ± 1.2	0.05
cv score - mean ± SD	1.7 ± 1.0	1.1 ± 1.0	NS	1.7 ± 0.9	1.4 ± 1.1	NS
C4d deposition - n (%)	7 (77.8)	21 (80.8)	NS	4 (16.7)	15 (53.6)	0.006

cg, allograft glomerulopathy; cv, vascular fibrous intimal thickening; eGFR, estimated glomerular filtration rate; g, glomerulitis; i, mononuclear cell interstitial inflammation; IF/TA, interstitial fibrosis/tubular atrophy; ptc, peritubular capillaritis; t, tubulitis; v, intimal arteritis

*Time between transplantation and allograft biopsy with concomitant anti-HLA antibodies assessment

Supplementary Table 4. Clinical and histological characteristics according to the IgG1 status in the recipients with antibody-mediated injury.

	IgG1 positive N=73	IgG1 negative N=14	p-value
Clinical characteristics			
Time to diagnosis* (d) - median (Q1-Q3)	79 (18-363)	353 (37-370)	NS
eGFR at biopsy (mL/min/1.73 m^2) - mean ± SD	34.4 ± 19.6	36.4 ± 13.7	NS
Time to failure (d) - median (Q1-Q3)	1033 (623-1655)	1013 (650-1777)	NS
Histological characteristics (Banff scores)			
g + ptc score - mean ± SD	3.5 ± 1.2	2.7 ± 0.9	0.03
i + t score - mean ± SD	1.2 ± 1.5	0.9 ± 1.6	NS
v score - mean ± SD	0.4 ± 0.8	0.5 ± 1.1	NS
cg score - mean ± SD	0.4 ± 0.8	0.07 ± 0.3	NS
IF/TA score - mean ± SD	1.0 ± 1.1	1.1 ± 1.1	NS
cv score - mean ± SD	1.3 ± 1.0	1.7 ± 1.1	NS
C4d deposition - n (%)	43 (58.9)	4 (28.6)	0.04

cg, allograft glomerulopathy; cv, vascular fibrous intimal thickening; eGFR, estimated glomerular filtration rate; g, glomerulitis; i, mononuclear cell interstitial inflammation; IF/TA, interstitial fibrosis/tubular atrophy; ptc, peritubular capillaritis; t, tubulitis; v, intimal arteritis
*Time between transplantation and allograft biopsy with concomitant anti-HLA antibodies assessment

Supplementary Table 5. Clinical and histological characteristics according to the IgG2 status in the recipients with antibody-mediated injury.

	IgG2 positive N=52	IgG2 negative N=35	p-value
Clinical characteristics			
Time to diagnosis* (d) - median (Q1-Q3)	249 (20-366)	67 (18-358)	NS
eGFR at biopsy (mL/min/1.73 m^2) - mean ± SD	36.3 ± 20.8	32.4 ± 15.2	NS
Time to failure (d) - median (Q1-Q3)	1118 (623-1666)	835 (673-1115)	NS
Histological characteristics (Banff scores)			
g + ptc score - mean ± SD	3.4 ± 1.2	3.3 ± 1.2	NS
i + t score - mean ± SD	1.0 ± 1.3	1.5 ± 1.8	NS
v score - mean ± SD	0.3 ± 0.7	0.6 ± 1.0	0.08
cg score - mean ± SD	0.5 ± 0.8	0.2 ± 0.6	0.03
IF/TA score - mean ± SD	1.1 ± 1.1	0.9 ± 1.1	NS
cv score - mean ± SD	1.5 ± 1.0	1.3 ± 1.1	NS
C4d deposition - n (%)	31 (59.6)	16 (45.7)	NS

cg, allograft glomerulopathy; cv, vascular fibrous intimal thickening; eGFR, estimated glomerular filtration rate; g, glomerulitis; i, mononuclear cell interstitial inflammation; IF/TA, interstitial fibrosis/tubular atrophy; ptc, peritubular capillaritis; t, tubulitis; v, intimal arteritis
*Time between transplantation and allograft biopsy with concomitant anti-HLA antibodies assessment

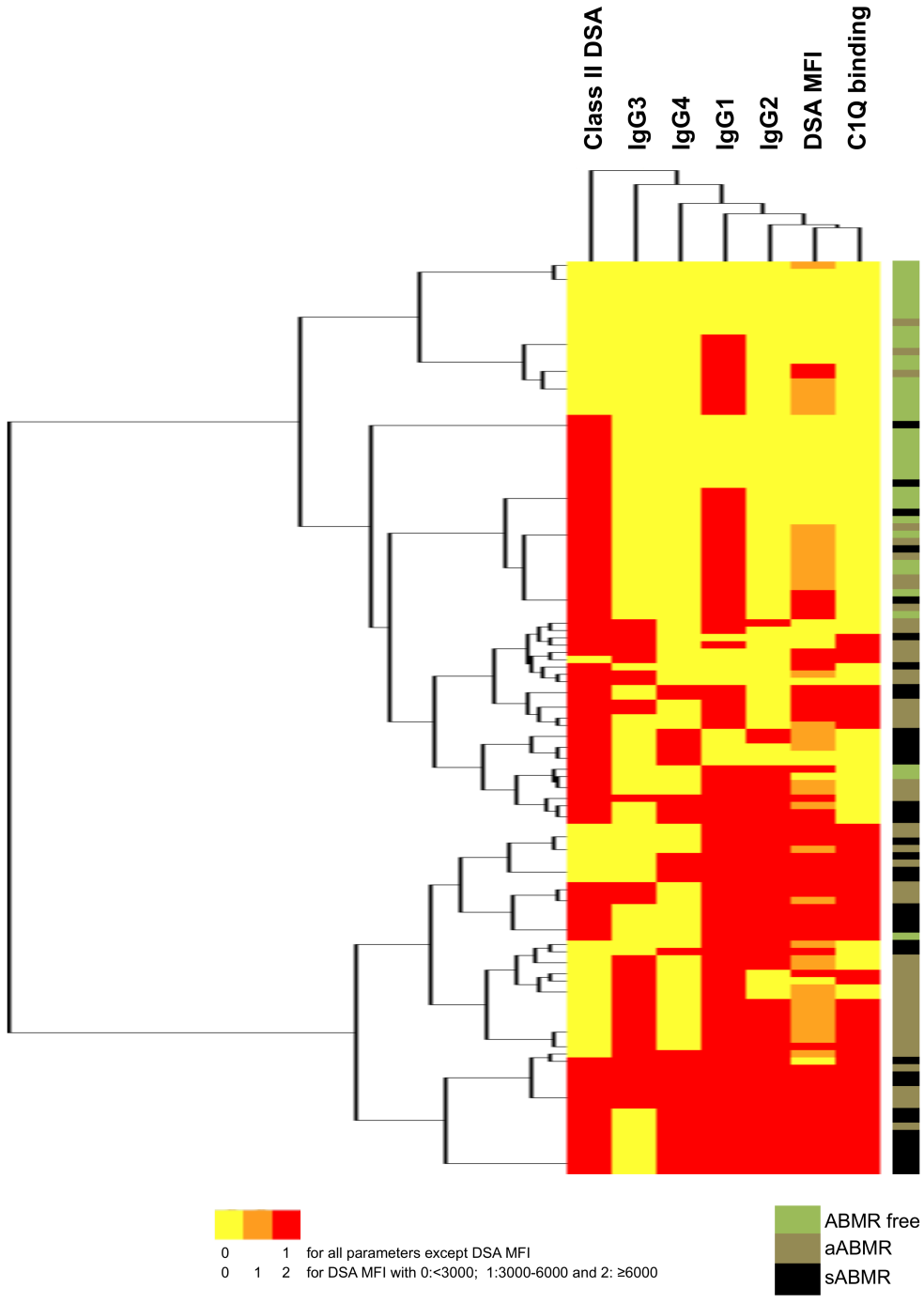
Supplementary Table 6. IgG subclass distribution according to the preformed/*de novo* status of the immunodominant donor-specific anti-HLA antibody.

IgG subclasses	Preformed iDSA N=98	*De novo* iDSA N=27	p-value
IgG1 - n (%)	76 (77.6)	18 (66.7)	NS
IgG2 - n (%)	44 (44.9)	11 (40.7)	NS
IgG3 - n (%)	29 (29.6)	6 (22.2)	NS
IgG4 - n (%)	24 (24.5)	9 (33.3)	NS

iDSA, immunodominant donor-specific antibody

Supplementary Figure 1. Distribution of the immunological variables (MFI, HLA class specificity, C1q-binding ability and IgG1-4 status) related to the dominant donor-specific anti-HLA antibody in the overall study population.

The heat map is colored according to positive (red) or negative (yellow) status for iDSA HLA class II, iDSA C1q-binding capacity, and iDSA IgG1-4. Two thresholds were used for MFI: <3000 (yellow), between 3000 and 6000 (orange), and >6000 (red).



SUPPLEMENTARY METHODS

Immunosuppression protocols

All patients received induction immunosuppressive therapy consisting of rabbit antithymocyte globulin (1.5 mg/kg/day for 10 days) or basiliximab (20 mg at day 0 and day 4). Maintenance immunosuppressive therapy consisted of prednisone, mycophenolate mofetil (1000 mg twice daily), tacrolimus administered to maintain a trough level of 8 to 10 ng/mL for the first 3 months and 6 to 8 ng/mL thereafter or cyclosporine administered to maintain a two-hour post-dose level of 800 to 1200 ng/mL for the first 3 months and 600 to 800 ng/mL thereafter. In addition, the patients considered at the highest immunological risk (preformed DSA by Luminex assay with MFI >3000 and historical positive CXM) received intravenous immunoglobulin (2 g/kg body weight on day 0, day 20, and day 40) with or without plasma exchanges.

Treatment of allograft rejections

All patients who had episodes of acute antibody-mediated rejection were equally treated with methylprednisolone pulses (500 mg/day for 3 days), intravenous immune globulin (2 g/kg, repeated every three weeks for 4 rounds), four plasmaphereses and two weekly doses of rituximab (375 mg/m^2 body-surface area).