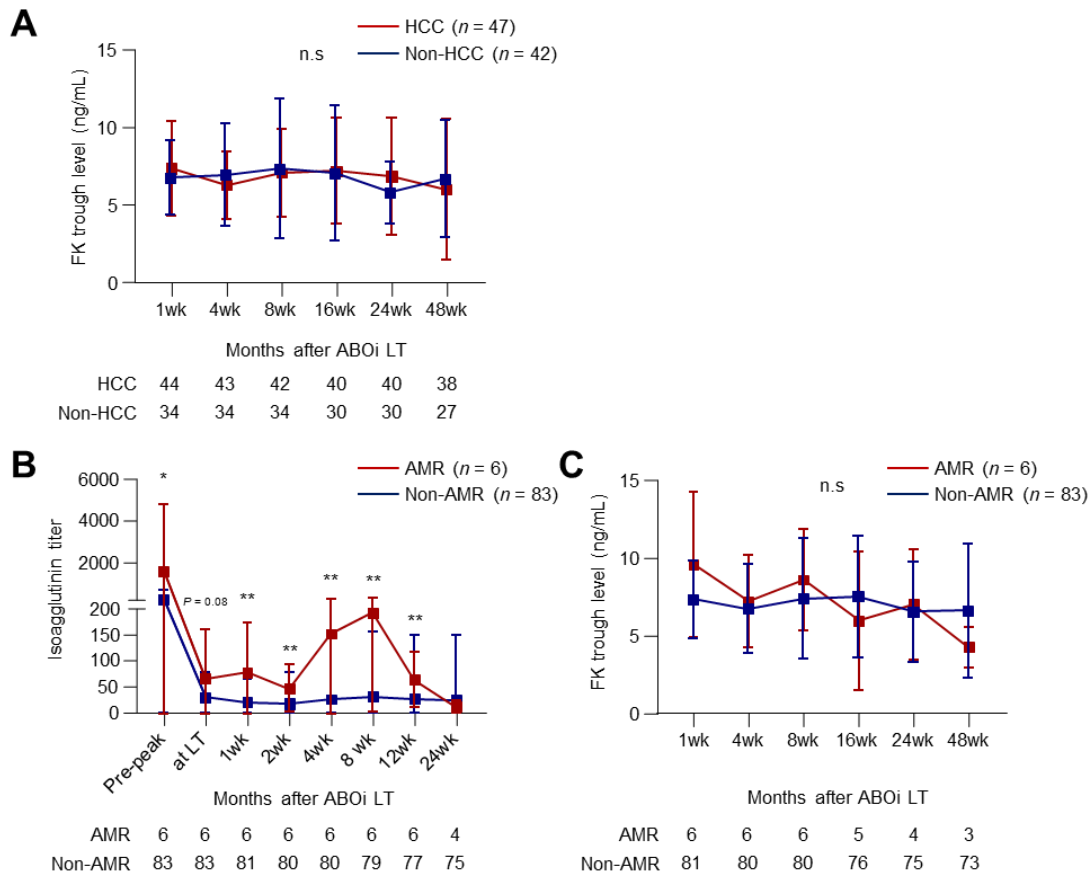


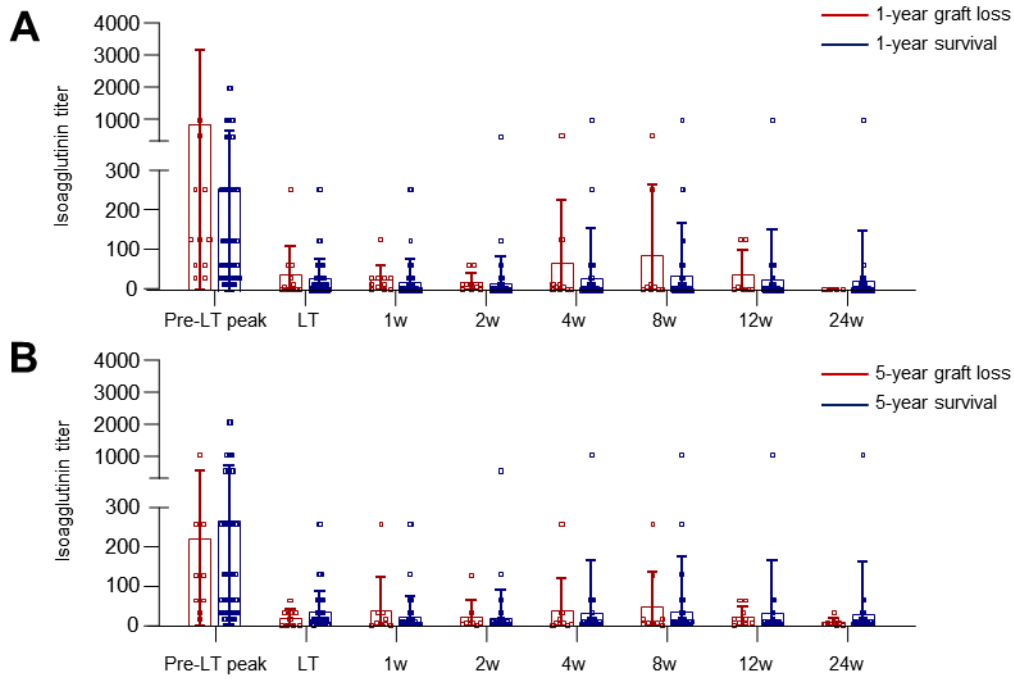
DOI: 10.4240/wjgs.v0.i0.0000 Copyright ©The Author(s) 2023.

**Supplementary Figure 1 Long-term outcomes of ABO-incompatible-liver transplantation patients.** A and B: Survival curves showing the graft survival of the total study group ( $n = 89$ ; A) and comparison between the hepatocellular carcinoma (HCC,  $n = 47$ ) and non-HCC ( $n = 42$ ) groups; C: Survival curve showing the overall survival in the HCC ( $n = 47$ ) and non-HCC ( $n = 42$ ) groups. ABOi: ABO-incompatible; HCC: Hepatocellular carcinoma; LT: Liver transplantation.



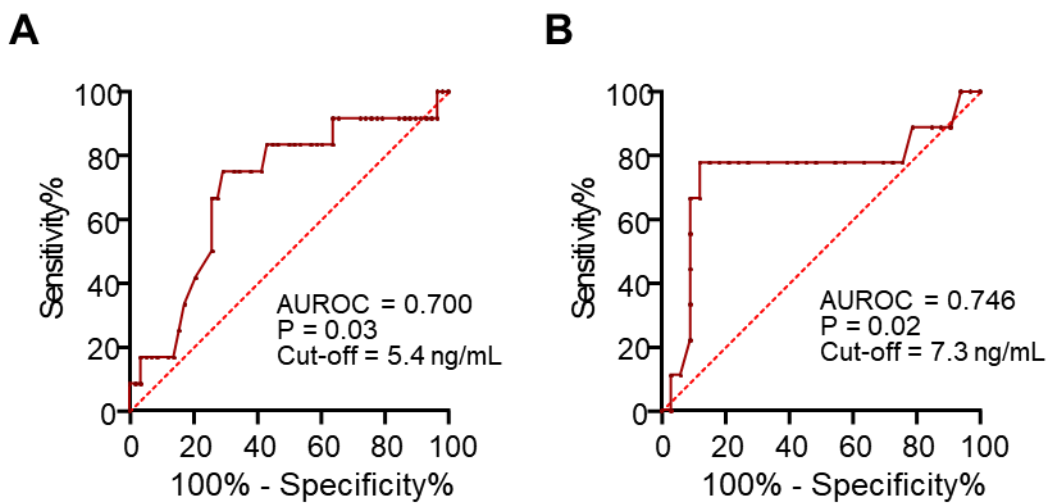
DOI: 10.4240/wjgs.v0.i0.0000 Copyright ©The Author(s) 2023.

**Supplementary Figure 2 Serial tacrolimus trough concentrations and isoagglutinin titers after ABO-incompatible liver transplantation.** A: Comparison of tacrolimus concentrations in hepatocellular carcinoma (HCC,  $n = 47$ ) and non-HCC ( $n = 42$ ) recipients at each time point; B: Comparison of isoagglutinin concentrations in the antibody-mediated rejection (AMR,  $n = 6$ ) and non-AMR ( $n = 83$ ) groups at each time point; C: Comparison of tacrolimus concentrations in the AMR ( $n = 6$ ) and non-AMR ( $n = 83$ ) groups at each time point. FK: Tacrolimus; HCC: Hepatocellular carcinoma; LT: Liver transplantation; AMR, antibody-mediated rejection; n.s.: Not significant. \*\*  $P < 0.01$ ; \*  $P < 0.05$ .



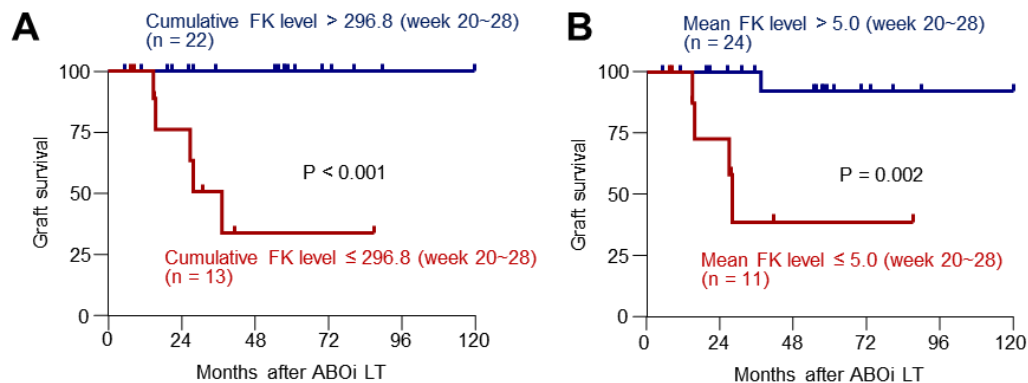
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**Supplementary Figure 3 Isoagglutinin titers before and after liver transplantation.** Isoagglutinin titers in each timepoint, patients were divided according to the 1-year graft loss (A) and 5-year graft loss (B). There was no statistical significance between graft loss and survival groups in every timepoints. W: Weeks; LT: Liver transplantation.



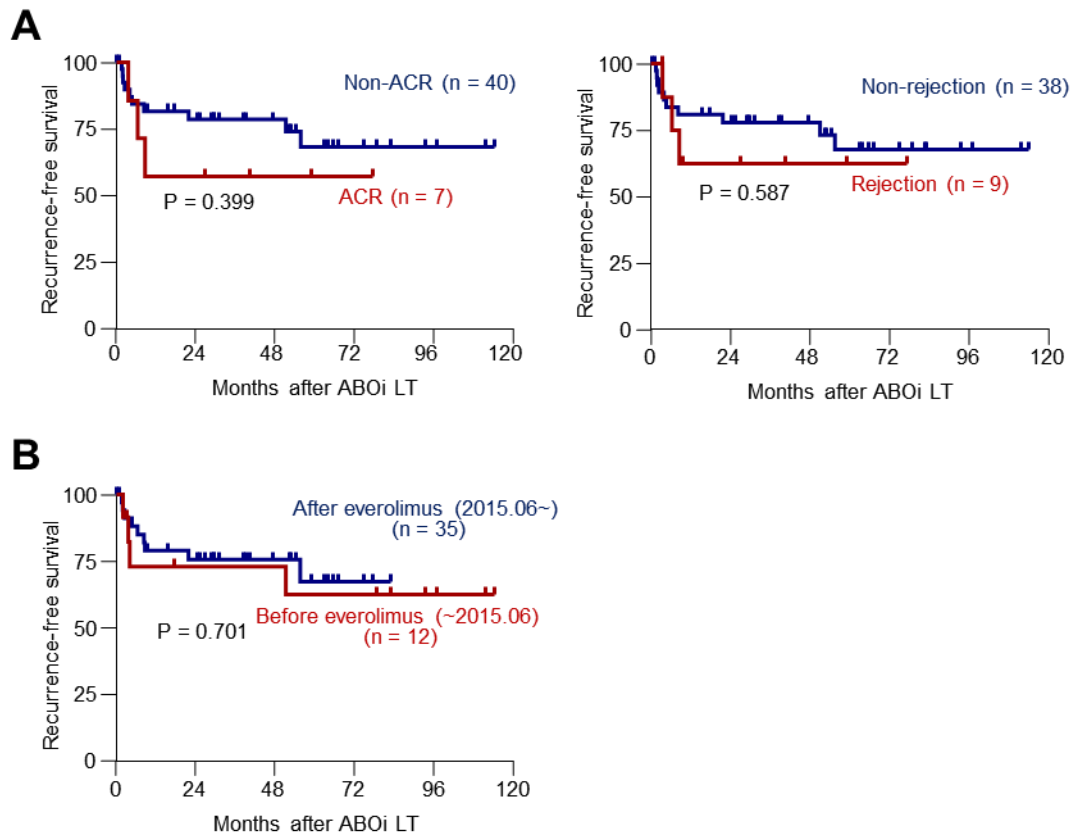
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**Supplementary Figure 4** Area under the receiver operating characteristic curves analyses for determining optimal cut-off points of serum tacrolimus level. Area under the receiver operating characteristic curves for serum tacrolimus level at 24 wk and graft-loss in total cohort ( $n = 89$ ) (A) and tacrolimus level at 4 wk and HCC recurrence in HCC subgroup ( $n = 47$ ) (B).



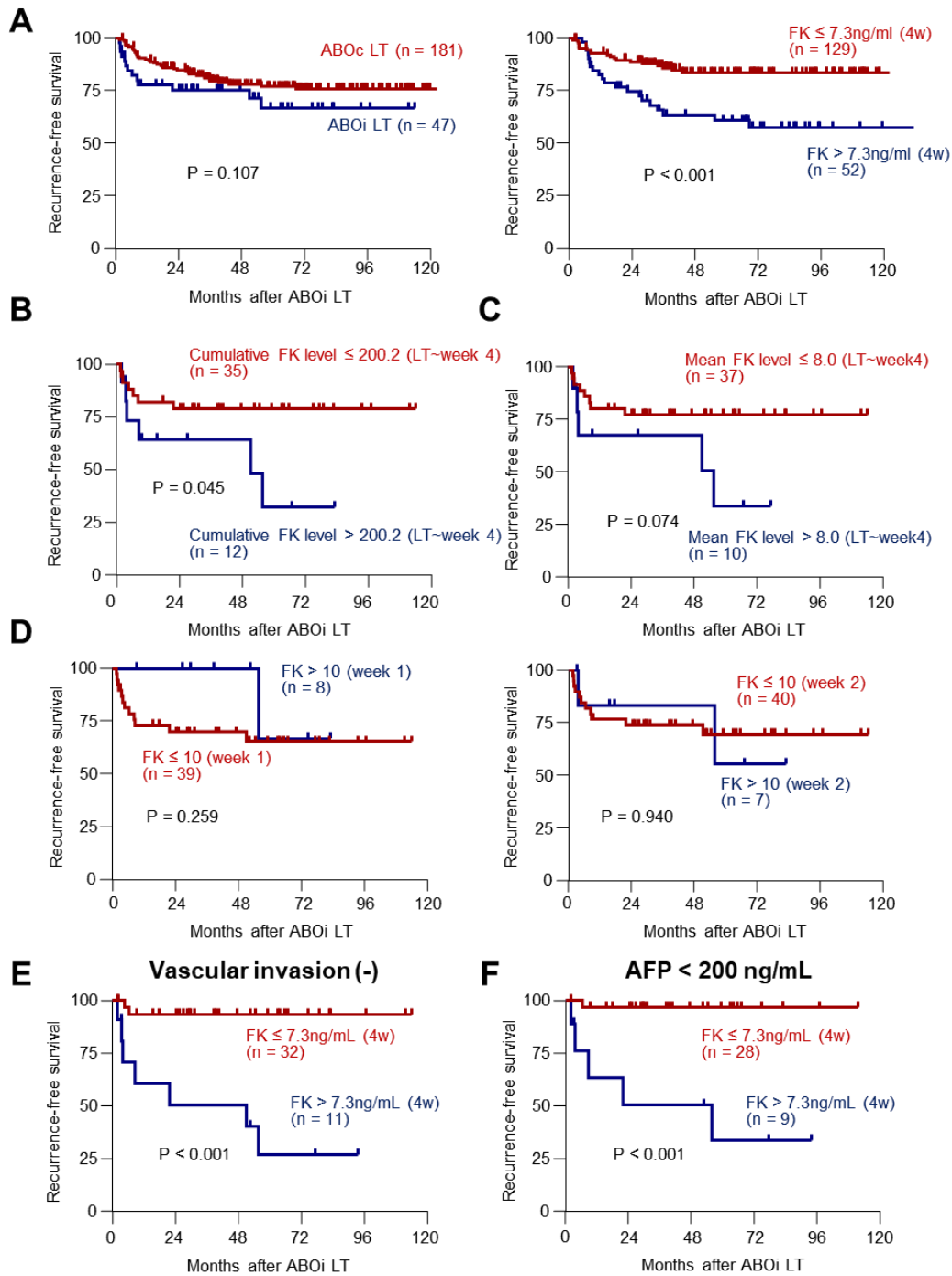
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**Supplementary Figure 5** Clinical outcome according to the serum tacrolimus level from week 20 to 28. A and B: Survival curves showing the graft survival according to the cumulative (A) and mean (B) tacrolimus level from week 20-28 after LT in non-hepatocellular carcinoma patients.



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**Supplementary Figure 6 Recurrence-free survival according to the rejection and transplantation timing.** A: Survival curves showing the difference of recurrence-free survival between acute cellular rejection (ACR) ( $n = 7$ ) and non-ACR ( $n = 40$ ), as well as total rejection (ACR + antibody-mediated rejection,  $n = 9$ ) and non-rejection ( $n = 38$ ); B: Survival curves showing the difference of recurrence-free survival between before ( $n = 12$ ) and after ( $n = 35$ ) everolimus groups.



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**Supplementary Figure 7 Recurrence-free survival according to the various clinical factors.** A: Survival curve showing the recurrence-free survival according to the ABO compatibility (A, left); B and C: Survival curve showing the recurrence-free survival according to the tacrolimus level at week 4 in ABO-compatible liver transplantation (LT) patients; Survival curve showing the recurrence-free survival according to the cumulative (B) mean tacrolimus level

(C) from the LT to 4 weeks after LT in patients with HCC; D: Survival curves showing the recurrence-free survival according to the tacrolimus level with cut-off 10 ng/mL at week 1 and week 2; E and F: Recurrence-free survival in the subgroups without vascular invasion (E) and low AFP level (F).

**Supplementary Table 1 Comparison of baseline characteristics according to the 1-year or 5-year graft loss**

	<b>1-year loss n = 79</b>	<b>non-1-year graft loss n = 10</b>	<b>p</b>	<b>5-year loss n = 69</b>	<b>non-5-year graft loss n = 20</b>	<b>P value</b>
Male gender	59 (74.7)	5 (50.0)	0.207	53 (76.8)	11 (55.0)	0.103
Age, years	55.0 [50.0;60.0]	51.5 [46.0;54.0]	0.054	55.0 [50.0;60.0]	52.5 [44.0;59.0]	0.148
Donor age, years	41.0 [27.5;54.0]	29.5 [21.0;48.0]	0.075	42.0 [27.0;54.0]	35.5 [28.5;47.5]	0.224
Graft type, right	73 (92.4)	10 (100.0)	0.816	63 (91.3)	20 (100.0)	0.39
Graft volume	786.0 [657.5;873.5]	853.5 [746.0;976.0]	0.231	800.0 [674.0;917.3]	864.5 [745.5;960.0]	0.238
Graft-recipient weight ratio (%)	1.2 [1.0; 1.3]	1.4 [1.0; 1.6]	0.14	1.1 [1.0; 1.3]	1.3 [1.1; 1.5]	0.072
Etiology			0.332			0.447
HBV	42 (53.2)	8 (80.0)		38 (55.1)	12 (60.0)	
HCV	8 (10.1)	0 (0.0)		7 (10.1)	1 (5.0)	
Alcohol	23 (29.1)	1 (10.0)		20 (29.0)	4 (20.0)	
Others	6 (7.6)	1 (10.0)		4 (5.8)	3 (15.0)	
HCC	42 (53.2)	5 (50.0)	1	37 (53.6)	10 (50.0)	0.975
Pre-operative laboratory tests						

	<b>1-year loss <i>n</i> = 79</b>	<b>non- 1-year graft loss <i>n</i> = 10</b>	<b>p</b>	<b>5-year loss <i>n</i> = 69</b>	<b>non- 5-year graft loss <i>n</i> = 20</b>	<b><i>P</i> value</b>
WBC, 10 <sup>9</sup> /L	4.9 [3.5; 6.8]	4.4 [2.4; 7.7]	0.479	4.8 [3.5; 7.4]	5.0 [2.8; 7.1]	0.572
Hemoglobin, g/dL	10.3 [8.7;12.6]	8.4 [7.8;11.9]	0.119	10.3 [8.6;12.6]	9.5 [8.0;11.8]	0.295
Platelet, 10 <sup>9</sup> /L	81.0 [51.0;127.0]	57.5 [44.0;122.0]	0.388	81.0 [51.0;124.0]	76.0 [44.5;135.5]	0.902
Creatinine, mg/dL	0.8 [0.7; 0.9]	0.8 [0.7; 0.9]	0.866	0.8 [0.7; 0.9]	0.8 [0.6; 0.9]	0.579
Albumin, g/dL	3.4 [3.0; 3.8]	3.6 [2.9; 3.8]	0.83	3.4 [2.9; 3.7]	3.5 [3.0; 3.8]	0.775
AST, U/L	38.0 [26.0;60.0]	26.5 [21.0;52.0]	0.247	36.0 [26.0;54.0]	49.5 [23.0;92.5]	0.47
ALT, U/L	23.0 [16.0;42.0]	18.0 [15.0;20.0]	0.219	22.0 [15.0;33.0]	26.5 [18.0;73.5]	0.067
ALP, U/L	69.0 [50.0;93.5]	55.5 [43.0;58.0]	0.125	68.0 [50.0;94.0]	58.0 [46.5;80.5]	0.455
Total bilirubin, mg/dL	1.4 [0.7; 5.4]	1.0 [0.7; 2.3]	0.278	1.4 [0.7; 3.7]	1.0 [0.7; 3.8]	0.764
γ-GTP, U/L	39.0 [22.0;79.0]	27.5 [19.0;51.0]	0.36	36.0 [21.0;57.0]	51.0 [26.5;77.0]	0.23
INR	1.4 [1.1; 1.7]	1.3 [1.1; 1.4]	0.953	1.3 [1.1; 1.7]	1.3 [1.1; 1.7]	0.871
Sodium, mmol/mL	141.0 [138.0;142.0]	140.5 [140.0;142.0]	0.85	141.0 [138.0;142.0]	141.0 [139.5;142.5]	0.429
Child-Pugh score	7.0 [5.0;10.0]	6.0 [5.0; 8.0]	0.36	7.0 [5.0;10.0]	6.0 [5.0;10.5]	0.501
MELD score	12.0 [8.0;19.0]	9.5 [8.0;14.0]	0.465	12.0 [8.0;19.0]	10.0 [8.0;17.0]	0.737



	1-year non-loss <i>n</i> = 79	1-year graft loss <i>n</i> = 10	<i>p</i>	5-year non-loss <i>n</i> = 69	5-year graft loss <i>n</i> = 20	<i>P</i> value
MELD-Na score	13.0 [8.0;20.5]	9.5 [8.0;14.0]	0.523	13.0 [8.0;20.0]	10.0 [8.0;18.0]	0.615
Crossmatching, positive	72 (91.1)	5 (50.0)	0.002	62 (89.9)	15 (75.0)	0.18
PRA, positive	38 (48.1)	3 (30.0)	0.456	32 (46.4)	9 (45.0)	1
HLA-A mismatch	61 (77.2)	7 (70.0)	0.912	55 (79.7)	13 (65.0)	0.287
HLA-B mismatch	64 (81.0)	6 (60.0)	0.263	49 (84.5)	14 (66.7)	0.154
HLA-C mismatch	55 (69.6)	8 (80.0)	0.756	48 (69.6)	15 (75.0)	0.848
HLA-DR mismatch	64 (81.0)	9 (90.0)	0.795	58 (84.1)	15 (75.0)	0.55
HLA mismatch, number	4.0 [3.0; 6.0]	3.5 [3.0; 4.0]	0.653	4.0 [3.0; 6.0]	3.5 [1.5; 6.5]	0.465
CD19, %	0.2 [0.1; 0.7]	0.3 [0.1; 0.5]	0.974	0.2 [0.1; 0.5]	0.3 [0.2; 0.8]	0.224
CD20, %	0.0 [0.0; 0.0]	0.0 [0.0; 0.1]	0.649	0.0 [0.0; 0.0]	0.0 [0.0; 0.1]	0.412
Isoagglutinin titer,						
Pre-LT, peak	128.0 [32.0;256.0]	128.0 [64.0;256.0]	0.563	128.0 [32.0;256.0]	128.0 [64.0;256.0]	0.716
At LT	16.0 [3.0;32.0]	6.0 [4.0;32.0]	0.713	16.0 [4.0;32.0]	12.0 [3.0;32.0]	0.662
Post-LT, peak	16.0 [8.0;32.0]	16.0 [8.0;64.0]	0.631	16.0 [4.0;32.0]	16.0 [12.0;64.0]	0.173

		1-year non- loss <i>n</i> = 79	1-year graft loss <i>n</i> = 10	<i>p</i>	5-year non- loss <i>n</i> = 69	5-year graft loss <i>n</i> = 20	<i>P</i> value
Tacrolimus concentration, ng/mL, trough level							
Post-LT week	1	6.6 [4.9; 8.7]	7.2 [6.4; 8.2]	0.405	6.4 [4.8; 8.7]	7.2 [5.8; 8.2]	0.287
Post-LT week	4	5.9 [4.3; 7.4]	8.7 [6.3; 9.7]	0.012	6.0 [4.4; 7.3]	7.3 [4.8; 9.4]	0.308
Post-LT week	8	6.6 [5.3; 8.7]	8.1 [3.1; 8.8]	0.654	6.6 [5.4; 8.8]	6.5 [4.5; 8.7]	0.757
Post-LT week	16	6.4 [4.8; 9.0]	2.3 [0.0; 6.6]	0.083	6.2 [4.6; 9.9]	6.3 [4.6; 7.5]	0.397
Post-LT week	24	7.1 [ 5.4; 9.1]	7.2 [ 5.8; 8.4]	0.741	6.2 [4.9; 7.5]	5.1 [4.3; 5.9]	0.057
Post-LT week	48	5.5 [3.9; 7.3]			5.7 [4.1; 7.5]	4.0 [3.5; 7.8]	0.534
ACR		14 (17.7)	2 (20.0)	1	10 (14.5)	6 (30.0)	0.208
AMR		3 (3.8)	3 (30.0)	0.015	1 (1.4)	5 (25.0)	0.001
Biliary stricture		30 (38.0)	6 (60.0)	0.32	24 (34.8)	12 (60.0)	0.078
Hepatic artery thrombosis		5 (6.3)	2 (20.0)	0.374	5 (7.2)	2 (10.0)	1
Rituximab, 375mg/m <sup>2</sup>		59 (88.1)	7 (70.0)	0.299	51 (87.9)	15 (78.9)	0.553
mTOR inhibitor		15 (19.0)	3 (30.0)	0.69	10 (14.5)	8 (40.0)	0.029
Graft loss at the later timepoint		10 (12.7)	10 (100.0)	< 0.001	0 (0.0)	20 (100.0)	< 0.001

	1-year loss <i>n</i> = 79	non- 1-year graft loss <i>n</i> = 10	<i>p</i>	5-year loss <i>n</i> = 69	non- 5-year graft loss <i>n</i> = 20	<i>P</i> value
Re-transplantation	0 (0.0)	2 (20.0)	0.004	0 (0.0)	2 (10.0)	0.072
Observation periods, days	1140.0 [473.0;2015.0]	125.0 [86.0;264.0]	< 0.001	1441.0 [594.0;2134.0]	368.0 [125.0;509.5]	< 0.001

Data are given as *n* (%) or mean ± SD. HBV, hepatitis B virus; HCV, hepatitis C virus; HCC, hepatocellular carcinoma; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase;  $\gamma$ -GTP, gamma glutamyl transpeptidase; INR, international normalized ratio; MELD, model for end-stage liver disease; PRA, panel reactive antibody; HLA, human leukocyte antigen; LT, liver transplantation; ACR, acute cellular rejection; AMR, antibody mediated rejection.

**Supplementary Table 2 Univariate and multivariate logistic regression analyses of factors associated with antibody mediated rejection**

	Univariate		Multivariate		<i>P</i> value
	OR (95% CI)	<i>P</i>	OR (95% CI)		
B cell crossmatching, positive	0.14 (0.02-0.83)	0.024			n.s.
Tacrolimus level, post-LT 1 week	1.38 (1.04-1.88)	0.028			n.s.
Isoagglutinin titer, post-LT, peak	1.00 (1.00-1.01)	0.010	1.00 (1.00-1.01)		0.022

OR, Odds ratio; CI, confidence interval; HLA, human leukocyte antigen; n.s., not significant.

**Supplementary Table 3 Summary of recipients with graft loss**

Cas	Tacrolimu	Tacrolimu	AM	HC	Observatio	Cause	of
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e no.	s level, post-LT 4w, ng/mL	s level, post-LT 24w, ng/mL	R	C	n time, days	graft loss
1	9.2	0	No	Yes	264	HCC recurrence Hepatic
2	2.8	3	Yes	No	817	failure d/t AMR Hepatic
3	5.5	4.2	No	No	472	failure d/t ACR Hepatic
4	3.8	4.3	No	No	451	failure d/t ACR
5	2.2	4.4	No	Yes	419	HCC recurrence
6	9.6	4.9	No	No	1137	Sudden death
7	7.7	5.1	No	Yes	340	HCC recurrence Sepsis
8	2.8	5.1	No	Yes	474	(extrahepatic )
9	11.6	5.3	No	No	851	CCC progression
10	9.3	6	No	Yes	545	HCC recurrence Hepatic
11	6.3	7.3	Yes	Yes	288	failure d/t AMR

12	7.3	11.6	Yes	Yes	814	Biliary sepsis
13	15.2	NA	No	No	90	Biliary sepsis
14	9.7	NA	Yes	Yes	100	Hepatic failure d/t AMR
15	8.7	NA	No	Yes	262	HCC recurrence
16	12.6	NA	No	No	77	Sepsis (extrahepatic)
17	NA	NA	No	Yes	9	Post op. complication Sepsis
18	6.8	NA	No	Yes	31	(extrahepatic)
19	6.1	NA	No	No	86	Biliary sepsis
20	5.7	NA	Yes	No	150	Sepsis (extrahepatic)
21	NA	NA	No	No	1	Post op. complication
22	4.7	5.9	No	Yes	396	HCC recurrence

AMR, antibody mediated rejection; HCC, hepatocellular carcinoma; ACR, acute cellular rejection, CCC, cholangiocarcinoma; NA, not available; op., operation.

**Supplementary Table 4 Comparison of baseline characteristics between recipients without and with hepatocellular carcinoma**

	Non-HCC ( <i>n</i> = 42)	HCC ( <i>n</i> = 47)	<i>P</i> value
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Male gender	24 (57.1)	40 (85.1)	0.007
Age	52.0 [46.0;57.0]	57.0 [52.5;61.0]	0.009
Donor age, years	41.5 [28.0;52.0]	36.0 [27.0;53.0]	0.601
Etiology			<
			0.001
HBV	13 (31.0)	37 (78.7)	
HCV	3 (7.1)	5 (10.6)	
Alcohol	19 (45.2)	5 (10.6)	
Others	7 (16.7)	0 (0.0)	
Pre-operative laboratory tests			
WBC, 10 <sup>9</sup> /L	5.6 [3.9; 8.3]	4.4 [3.1; 5.8]	0.042
Hemoglobin, g/dL	9.4 [8.2;10.2]	11.4 [8.9;13.3]	<
Platelet, 10 <sup>9</sup> /L	66.5 [45.0;124.0]	88.0 [54.5;127.0]	0.44
Creatinine, mg/dL	0.7 [0.6; 0.9]	0.8 [0.7; 0.9]	0.008
Albumin, g/dL	3.2 [2.5; 3.6]	3.6 [3.2; 4.0]	<
AST, U/L	45.0 [29.0;64.0]	32.0 [24.0;49.0]	0.031
ALT, U/L	19.5 [14.0;33.0]	24.0 [18.0;42.0]	0.225
ALP, U/L	71.5 [56.0;103.0]	57.0 [43.5;75.0]	0.01
Total bilirubin, mg/dL	2.9 [1.2; 8.4]	0.8 [0.6; 1.4]	<
γ-GTP, U/L	36.5 [19.0;89.0]	41.0 [27.5;51.5]	0.739
INR	1.6 [1.3; 1.8]	1.2 [1.1; 1.4]	<
Sodium, mmol/mL	140.0 [136.0;142.0]	141.0 [139.0;143.0]	0.028
Child-Pugh score	10.0 [6.0;12.0]	6.0 [5.0; 7.0]	<
			0.001
MELD score	15.5 [12.0;23.0]	9.0 [7.0;11.5]	<
			0.001

HLA crossmatching, positive	34 (81.0)	43 (91.5)	0.253
HLA-A mismatch	32 (76.2)	36 (76.6)	1
HLA-B mismatch	30 (71.4)	40 (85.1)	0.189
HLA-C mismatch	27 (64.3)	36 (76.6)	0.298
HLA-DR mismatch	33 (78.6)	40 (85.1)	0.6
HLA mismatch, number	3.0 [3.0; 6.0]	4.0 [3.0; 6.0]	0.273
PRA, positive	22 (52.4)	19 (40.4)	0.359
CD19,	0.3 [0.1; 1.7]	0.2 [0.1; 0.4]	0.068
CD20,	0.0 [0.0; 0.1]	0.0 [0.0; 0.0]	0.06
Isoagglutinin titer,			
Pre-LT, peak	128.0 [64.0;256.0]	64.0 [32.0;256.0]	0.78
At LT	16.0 [4.0;32.0]	16.0 [4.0;32.0]	0.816
Post-LT, peak	16.0 [8.0;64.0]	16.0 [4.0;32.0]	0.623
Tacrolimus concentration, ng/mL, trough level			
Post-LT 1 week	6.6 [5.2; 7.8]	6.8 [4.9; 8.8]	0.616
Post-LT 4 week	6.2 [4.8; 8.4]	6.0 [4.3; 7.9]	0.517
Post-LT 8 week	6.6 [4.8; 8.8]	6.6 [5.6; 8.7]	0.877
Post-LT 16 week	6.0 [4.0;10.9]	6.5 [5.0; 8.4]	0.499
Post-LT 24 week	5.9 [4.5; 6.8]	6.2 [4.7; 7.6]	0.371
Post-LT 48 week	6.3 [4.2; 9.1]	5.2 [3.7; 6.8]	0.113
ACR	9 (21.4)	7 (14.9)	0.6
AMR	3 (7.1)	3 (6.4)	1
Biliary stricture	17 (40.5)	19 (40.4)	1
Hepatic artery thrombosis	5 (11.9)	2 (4.3)	0.345
Rituximab, 375mg/m <sup>2</sup>	30 (85.7)	36 (85.7)	1
mTOR inhibitor	5 (11.9)	13 (27.7)	0.113
Graft loss	10 (23.8)	10 (21.3)	0.975
Re-transplantation	0 (0.0)	2 (4.3)	0.525
De novo malignancy	1 (2.7)	1 (2.1)	1

Over Milan criteria		18 (38.3)	
HCC recurrence		13 (27.7)	
Observation periods, days	716.0 [257.0;1749.0]	1200.0 [507.0;2155.0]	0.038

Data are given as n (%) or median [interquartile]. HBV, hepatitis B virus; HCV, hepatitis C virus; HCC, hepatocellular carcinoma; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase;  $\gamma$ -GTP, gamma glutamyl transpeptidase; INR, international normalized ratio; MELD, model for end-stage liver disease; PRA, panel reactive antibody; HLA, human leukocyte antigen; LT, liver transplantation; ACR, acute cellular rejection; AMR, antibody mediated rejection.

**Supplementary Table 5 Comparison of baseline tumor burden of hepatocellular carcinoma patients between recurrence and non-recurrence groups**

	Non-recurrence ( <i>n</i> = 34)	Recurrence ( <i>n</i> = 13)	<i>P</i> value
Pre-LT treatment	13 (38.2)	6 (46.2)	0.871
TACE	13 (38.2)	4 (30.8)	
Hepatectomy	0 (0)	2 (15.4)	
Baseline characteristics before pre-LT treatment			
Largest tumor size, cm	2.6 [1.7; 3.8]	3.9 [2.7; 4.0]	0.147
Tumor number	2.0 [1.0; 2.0]	1.0 [1.0; 2.0]	0.344
Vascular invasion	0 (0.0)	3 (50.0)	0.036
AFP, ng/mL	11.6 [2.6;23.9]	875.4 [155.0;2163.0]	0.032
Baseline characteristics before LT			



Largest tumor size, cm	1.5 [0.0; 3.0]	3.3 [1.6; 4.5]	0.082
Tumor number	1.0 [0.0; 2.0]	1.0 [1.0; 2.0]	0.201
Vascular invasion	0 (0.0)	4 (30.8)	0.005
AFP, ng/mL	11.8 [3.2;24.7]	28.8 [13.0;498.7]	0.015

Data are given as *n* (%) or median [interquartile]. LT, liver transplantation; TACE, transarterial chemoembolization; AFP, alpha-fetoprotein.