

**Supplementary Table 1. Comparison of causes of death of patients with or without HCC recurrence after receiving a liver transplant at the University Medical Center Mainz between 1998 and 2017.**

	Patients		p-value
	Without recurrence (n=96)	With recurrence (n=37)	
Cardiovascular disease	16	1	<b>0.031</b>
De novo malignancy	16	0	<b>0.008</b>
Recurrence of the liver disease	9	1	0.191
HCC recurrence	0	34	<b>&lt;0.001</b>
Infections	22	0	<b>0.001</b>
Others	33	1	<b>&lt;0.001</b>

Note: Information on the cause of death was available for 133 of 142 deceased patients.

**Supplementary Table 2. Comparison of additional baseline characteristics of patients with or without HCC recurrence after receiving a liver transplant at the University Medical Center Mainz between 1998 and 2017 (n=304).**

	Patients		p-value
	Without recurrence (n=253)	With recurrence (n=51)	
<b>Blood group</b>			
- 0	88 (35%)	14 (27%)	0.399
- A	118 (47%)	28 (55%)	
- B	36 (14%)	5 (10%)	
- AB	11 (4%)	4 (8%)	
<b>Pretreatments other than TACE and resection</b>			
SIRT	1 (0%)	1 (2%)	0.207
IRE	2 (1%)	1 (2%)	0.441
PEI	13 (5%)	3 (6%)	0.828
Sorafenib	2 (1%)	1 (2%)	0.441
RFA	13 (5%)	3 (6%)	0.828
<b>Etiologies other than alcohol and viral hepatitis</b>			
Haemochromatosis	9 (4%)	3 (6%)	0.437
NASH	3 (1%)	3 (6%)	<b>0.028</b>
AIH	2 (1%)	1 (2%)	0.441
PBC	9 (4%)	0 (0%)	0.172
PSC	1 (0%)	0 (0%)	0.653
<b>Immunosuppression</b>			
Tacrolimus	241 (95%)	47 (92%)	0.366
Cyclosporine	11 (4%)	4 (8%)	0.293
Everolimus	18 (7%)	2 (4%)	0.401
Sirolimus	10 (4%)	3 (6%)	0.534
MMF	153 (60%)	23 (45%)	<b>0.042</b>
Simulect	10 (4%)	1 (2%)	0.487
Imurek	4 (2%)	2 (4%)	0.273
mTOR inhibitor	28 (11%)	5 (10%)	0.791

P-values smaller than 0.05 are considered to be statistically significant and are highlighted in bold.

**Supplementary Table 3. Comparison of baseline characteristics of patients with early or late HCC recurrence (defined as diagnosed  $\leq$  or  $>$  2 years after LT; n=51).**

	Early recurrence (n=26)	Late recurrence (n=25)	p-value
Alive	2 (8%)	9 (36%)	<b>0.014</b>
Time to last follow-up/death (years)	1.45 (0.62-2.97)	6.18 (4.49-8.43)	<b>&lt;0.001</b>
Recurrence-free survival (years)	0.79 (0.40-1.18)	3.71 (3.15-4.94)	<b>&lt;0.001</b>
Survival free of intrahepatic recurrence (days)	1.26 (0.62-1.84)	5.41 (4.39-7.05)	<b>&lt;0.001</b>
Survival free of extrahepatic recurrence (days)	0.96 (0.39-1.28)	3.71 (3.15-4.99)	<b>&lt;0.001</b>
Time from recurrence until death (days)	237.5 (112.0-640.0)	430.5 (307.5-1212.5)	0.167
Time on the waiting list (days)	86.5 (55.0-337.0)	237.0 (89.0-304.0)	0.540
Time from HCC diagnosis until LT (days)*	298.0 (198.0-412.0)	330.0 (212.0-398.0)	0.977
DRI	1.435 (1.323-1.816)	1.818 (1.368-2.053)	0.176
Age	60.0 (53.7-63.4)	59.9 (54.2-64.1)	0.407
Male gender	16 (62%)	18 (72%)	0.428
LT before Dec 16, 2006 (pre MELD-era)	16 (62%)	13 (52%)	0.492
Cold ischemia time (minutes)	576.0 (450.0-671.0)	546.0 (473.0-689.5)	0.744
Outside Milan criteria (explant)	18 (69%)	11 (44%)	0.069
Outside Milan but inside UCSF criteria (explant)	17 (65%)	8 (32%)	<b>0.017</b>
Outside Milan but inside up-to-seven criteria (explant)	16 (62%)	7 (28%)	<b>0.016</b>
T stage (explant)			
- T0, T1 and T2	14 (54%)	22 (88%)	<b>0.007</b>
- T3 and T4	12 (46%)	3 (12%)	
Grading			
- G1	2 (8%)	5 (20%)	<b>0.041</b>
- G2	12 (46%)	16 (64%)	
- G3	12 (46%)	3 (12%)	
- Gx	0 (0%)	1 (4%)	
Number of tumour nodules			
- <3	9 (35%)	17 (68%)	<b>0.017</b>
- multifocal	17 (65%)	8 (32%)	
Nodule size >5 cm	8 (31%)	3 (12%)	0.103
Microvascular invasion	13 (50%)	3 (12%)	<b>0.003</b>
AFP (ng/mL) before LT	12.2 (5.1-236.0)	5.6 (3.0-10.7)	<b>0.011</b>
AFP (ng/mL) before TACE	132.5 (6.2-681.0)	10.3 (3.3-53.0)	<b>0.031</b>
AFP before LT >400 ng/mL	5 (15%)	1 (4%)	0.072
Absence of vital tumour tissue in the explant	2 (8%)	3 (12%)	0.605
Pretreatment			
- with TACE	20 (77%)	22 (88%)	0.300
- with resection	6 (23%)	2 (8%)	0.139
- other than resection or TACE	5 (19%)	3 (12%)	0.478
Number of TACE			
- 0	6 (23%)	3 (12%)	0.667
- 1 to 3	7 (27%)	7 (28%)	
- 4 to 6	8 (31%)	11 (44%)	
- 7 or more	5 (19%)	4 (16%)	
Modality of pre-LT HCC diagnosis			
- incidentaloma	1 (4%)	0 (0%)	0.186
- radiological evidence	6 (23%)	2 (8%)	
- histology	19 (73%)	23 (92%)	

Histological confirmation by liver biopsy	13 (50%)	21 (84%)	<b>0.010</b>
Etiology			
- Alcohol	11 (42%)	9 (36%)	0.645
- Hepatitis B	5 (19%)	5 (20%)	0.945
- Hepatitis B+D	2 (8%)	0 (0%)	0.157
- Hepatitis C	11 (42%)	8 (32%)	0.447
Child-Pugh class			
- Child A	10 (38%)	16 (64%)	0.361
- Child B	7 (27%)	5 (20%)	
- Child C	6 (23%)	4 (16%)	
MELD-score	11.0 (7.5-13.6)	9.0 (7.0-12.0)	0.325

Continuous variables are expressed as median with IQRs in brackets, categorical variables as n and frequencies (%). P-Values smaller than 0.05 are considered to be statistically significant and are highlighted in bold.

\*excluding patients with incidentalomas.

**Supplementary Table 4. Comparison of additional baseline characteristics of patients with early or late HCC recurrence (defined as diagnosed  $\leq$  or  $>$  2 years after LT; n=51).**

	Early recurrence (n=26)	Late recurrence (n=25)	p-value
<b>Blood group</b>			
- 0	8 (31%)	6 (24%)	0.894
- A	13 (50%)	15 (60%)	
- B	3 (12%)	2 (8%)	
- AB	2 (8%)	2 (8%)	
<b>Pretreatments other than TACE and resection</b>			
SIRT	0 (0%)	1 (4%)	0.303
IRE	1 (4%)	0 (0%)	0.322
PEI	1 (4%)	2 (8%)	0.529
Sorafenib	0 (0%)	1 (4%)	0.303
RFA	3 (12%)	0 (0%)	0.080
<b>Etiologies other than alcohol and viral hepatitis</b>			
Haemochromatosis	1 (4%)	2 (8%)	0.529
NASH	1 (4%)	2 (8%)	0.529
AIH	0 (0%)	1 (4%)	0.303
<b>T stage (explant)</b>			
- T0	2 (8%)	4 (16%)	0.091
- T1	3 (12%)	7 (28%)	
- T2	9 (35%)	11 (44%)	
- T3	11 (42%)	3 (12%)	
- T4	1 (4%)	0 (0%)	
<b>Number of tumour nodules</b>			
- 0	2 (8%)	3 (12%)	0.157
- 1	3 (12%)	9 (36%)	
- 2	2 (8%)	2 (8%)	
- 3	2 (8%)	3 (12%)	
- multifocal	17 (65%)	8 (32%)	
<b>Immunosuppression</b>			
Tacrolimus	25 (96%)	22 (88%)	0.279
Cyclosporine	1 (4%)	3 (12%)	0.279
Everolimus	1 (4%)	1 (4%)	0.977
Sirolimus	2 (8%)	1 (4%)	0.575
MMF	11 (42%)	12 (48%)	0.683
Simulect	0 (0%)	1 (4%)	0.303
Imurek	1 (4%)	1 (4%)	0.977
mTOR inhibitor	3 (12%)	2 (8%)	0.671

**Supplementary Table 5. Sites of HCC recurrence and their influence on survival.**

	Number of patients	Survival (years)	Log-rank p-value
Intra- vs. extrahepatic HCC recurrence (first manifestation)			
- intrahepatic recurrence	10 (20%)	2.8 (0.3-5.3)	0.86
- extrahepatic recurrence	36 (71%)	4.4 (3.1-5.7)	
- simultaneous recurrence	5 (10%)	5.8 (2.9-8.8)	
Intra- vs. extrahepatic HCC recurrence (any time-point)			
- intrahepatic recurrence	9 (18%)	3.0 (2.4-3.5)	0.65
- extrahepatic recurrence	27 (53%)	3.9 (2.4-5.4)	
- intra- and extrahepatic recurrence	15 (29%)	4.5 (3.5-5.5)	
Distinct sites			
- hepatic recurrence	24 (47%)	3.9 (1.7-6.1)	0.38
- pulmonary recurrence	26 (51%)	3.9 (2.4-5.4)	0.90
- bone recurrence	18 (35%)	3.3 (0.4-6.2)	0.49
- adrenal recurrence	10 (20%)	1.6 (0.8-2.4)	0.30
- lymph node recurrence	7 (14%)	3.4 (3.0-3.8)	0.35
- needle tract seeding	8 (16%)	9.7 (6.8-12.6)	<b>0.023</b>
- other recurrence	11 (22%)	5.8 (2.1-9.5)	0.75

Survival is expressed as years with 95% confidence intervals in brackets. Log-rank p-values smaller than 0.05 are considered to be statistically significant and are highlighted in bold.

**Supplementary Table 6. Sites of early and late HCC recurrence (defined as diagnosed  $\leq$  or  $>$  2 years after LT; n=51).**

	Early recurrence (n=26)	Late recurrence (n=25)	p-value
Intra- vs. extrahepatic HCC recurrence (first manifestation)			
- intrahepatic recurrence	7 (27%)	3 (12%)	0.388
- extrahepatic recurrence	17 (65%)	19 (76%)	
- simultaneous recurrence	2 (8%)	3 (12%)	
Intra- vs. extrahepatic HCC recurrence (any time-point)			
- intrahepatic recurrence	6 (23%)	3 (12%)	0.501
- extrahepatic recurrence	12 (46%)	15 (60%)	
- intra- and extrahepatic recurrence	8 (31%)	7 (28%)	
Distinct sites			
- hepatic recurrence	14 (54%)	10 (40%)	0.322
- pulmonary recurrence	13 (50%)	13 (52%)	0.886
- bone recurrence	11 (42%)	7 (28%)	0.285
- adrenal recurrence	7 (27%)	3 (12%)	0.180
- lymph node recurrence	4 (15%)	3 (12%)	0.725
- needle tract seeding	0 (0%)	8 (32%)	<b>0.002</b>
- other recurrence	5 (19%)	6 (24%)	0.679

P-values smaller than 0.05 are considered to be statistically significant and are highlighted in bold.