

Supplementary Material

Interleukin-8 and survival after transarterial radioembolization in hepatocellular carcinoma: a comprehensive study and external validation from the SORAMIC trial

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Supplementary Table S1: Baseline patients' characteristics of the SORAMIC study cohort treated with transarterial embolization in combination with sorafenib

Parameter	Patients (n=83)
Male sex (%)	77 (92.8%)
Median age (years) [†]	66 (44-81)
Liver cirrhosis (%)	71 (85.5%)
CTP class (%)	
A	64 (90.1%)
B	6 (8.5%)
ALBI score [†]	-2.66 (-3.39 - -1.56)
ALBI grade [†]	
1	42 (51.2%)
2	40 (48.8%)
BCLC stage (%)	
A	0 (0%)
B	26 (31.3%)
C	57 (68.7%)
IL-8 [pg/mL] [†]	53.60 (0.67-2591.35)
Albumin [g/L] [†]	39.1 (29.0-48.3)
Bilirubin [μmol/L] [†]	12.0 (3.0-42.8)
[†] median (range), ALBI: albumin-bilirubin, BCLC: Barcelona Clinic Liver Cancer, CTP: Child-Turcotte-Pugh, IL: interleukin, MELD: model for end-stage liver disease	

Supplementary Table S2: Association of baseline biochemical parameters, liver function scores and serum cytokine levels with survival beyond 12 weeks. Values are shown as median and range.

Parameter	Survival < 12 weeks after TARE (n=8)		Survival ≥ 12 weeks after TARE (n=70)		p-value
	Median	Range	Median	Range	
ALT [IU/L]	44	16-119	33	10-101	0.349
AP [IU/L]	157	101-301	141	47-653	0.472
GGT [IU/L]	311	35-799	201	47-1181	0.568
Leucocytes [10 ⁹ /L]	6.2	3.6-10.5	5.9	2.3-15.5	0.370
Hemoglobin [gm/dL]	7.7	4.2-9.0	8.1	5.6-10.7	0.187
Platelets [10 ⁹ /L]	144	52-219	129	40-512	0.695
Albumin [g/L]	37.2	26.5-44.8	39.3	26.1-47.1	0.235
Bilirubin [μmol/L]	14.4	6.2-59.5	12.8	3.8-43.8	0.444
Creatinine [μmol/L]	46	50-191	77	45-211	0.051
ALBI score	-2.49	-3.33--1.44	-2.72	-3.56--1.09	0.143
MELD Score	10	6-17	6	6-20	0.017
IL-1β [pg/mL]	5.77	2.42-377.00	9.28	1.50-548.31	0.536
IL-6 [pg/mL]	37.17	3.40-87.14	14.53	2.26-130.90	0.077
IL-8 [pg/mL]	309.80	44.49-6237.74	40.5	2.61-2034.06	7.40x10⁻⁴
IL-10 [pg/mL]	13.31	2.00-106.38	5.02	2.00-193.00	0.206
IL-12p70 [pg/mL]	3.08	2.00-90.47	3.08	2.00-51.88	0.753
IL-17a [pg/mL]	1.48	0.50-3.80	1.36	0.50-17.45	0.718
IL-18 [pg/mL]	280.47	93.40-1123.44	190.98	7.18-932.69	0.176
IL-23 [pg/mL]	11.61	3.07-129.35	5.78	1.80-157.30	0.273
IL-33 [pg/mL]	35.29	4.40-338.93	26.94	4.40-309.97	0.781
IFN-α2 [pg/mL]	12.48	2.10-58.74	3.91	2.10-45.58	0.067
IFN-γ [pg/mL]	6.23	1.30-19.89	6.78	1.59-76.01	0.688
TNF-α [pg/mL]	9.47	0.90-64.01	1161	0.90-338.16	0.989
MCP-1 [pg/mL]	236.93	73.59-3793.18	401.00	36.03-1191.08	0.752

ALBI: albumin-bilirubin, ALT: alanine aminotransferase, AST: aspartate aminotransferase, AP: alkaline phosphatase, GGT: gamma-glutamyl transpeptidase, IFN: interferon, IL: interleukin, MCP-1: monocyte chemoattractant protein-1, MELD: model for end-stage liver disease, TNF: tumor necrosis factor

Supplementary Table S3: Baseline biochemical parameters, liver function scores and serum cytokine levels with 24-week survival. Values are shown as median and range.

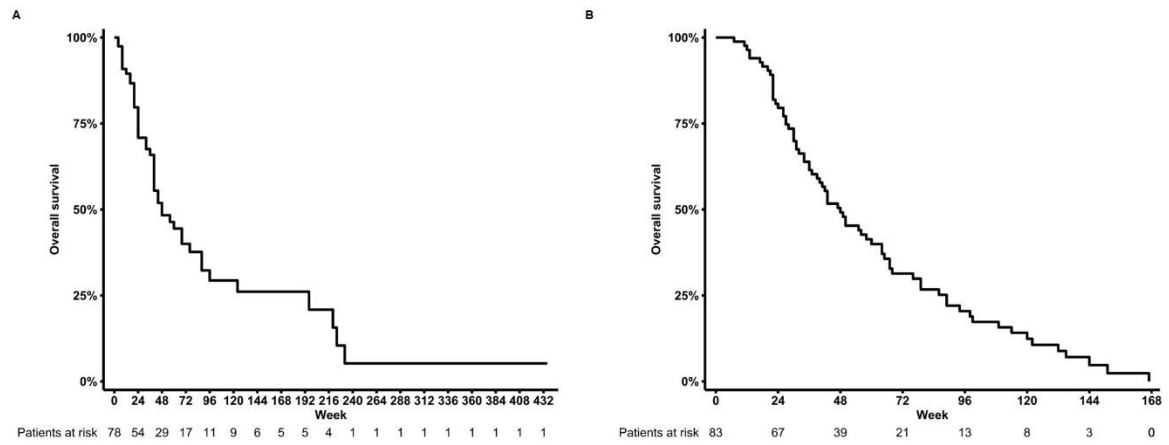
Parameter	Survival < 24 weeks after TARE (n=21)		Survival ≥ 24 weeks after TARE (n=57)		p-value
	Median	Range	Median	Range	
ALT [IU/L]	38	16-119	33	10-101	0.229
AP [IU/L]	152	81-653	143	47-452	0.358
GGT [IU/L]	272	35-1181	201	47-694	0.403
Leucocytes [10 ⁹ /L]	6.2	3.6-15.5	5.8	2.3-9.5	0.306
Hemoglobin [gm/dL]	7.8	4.2-9.3	8.2	5.6-10.7	0.112
Platelets [10 ⁹ /L]	146	40-302	127	51-512	0.435
Albumin [g/L]	38.4	27.2-47.1	39.2	26.1-47.0	0.288
Bilirubin [μmol/L]	12.5	6.2-59.5	13.2	3.8-43.8	0.425
Creatinine [μmol/L]	83	45-191	77	45-211	0.338
ALBI score	-2.64	-3.43--1.39	-2.72	-3.56--1.09	0.591
MELD Score	6	6-17	6	6-20	0.430
IL-1β [pg/mL]	5.28	2.42-377.00	10.67	1.50-548.31	0.021
IL-6 [pg/mL]	16.46	3.40-130.94	14.75	2.26-100.66	0.248
IL-8 [pg/mL]	142.36	2.62-6237.74	41.16	2.61-1185.60	0.289
IL-10 [pg/mL]	7.89	2.00-106.38	4.75	2.00-193.00	0.323
IL-12p70 [pg/mL]	3.60	2.00-90.47	3.08	2.00-51.88	0.756
IL-17a [pg/mL]	0.54	0.50-16.97	2.06	0.50-17.45	0.031
IL-18 [pg/mL]	253.07	7.18-1123.44	189.76	17.73-932.69	0.478
IL-23 [pg/mL]	8.75	1.80-157.30	5.30	1.80-146.97	0.923
IL-33 [pg/mL]	20.73	4.40-338.93	30.49	4.40-309.97	0.798
IFN-α2 [pg/mL]	7.71	2.10-58.74	4.11	2.10-45.58	0.561
IFN-γ [pg/mL]	8.15	1.30-31.63	6.44	1.59-76.01	0.736
TNF-α [pg/mL]	14.90	0.90-82.12	11.34	0.90-338.16	0.705
MCP-1 [pg/mL]	403.65	73.59-3793.18	395.18	36.03-1191.08	0.884

ALBI: albumin-bilirubin, ALT: alanine aminotransferase, AST: aspartate aminotransferase, AP: alkaline phosphatase, GGT: gamma-glutamyl transpeptidase, IFN: interferon, IL: interleukin, MCP-1: monocyte chemoattractant protein-1, MELD: model for end-stage liver disease, TNF: tumor necrosis factor

Supplementary TableS4: Patients' characteristics of the IL-8 ≤ 190 pg/ml and IL-8 >190pg/ml groups.

Parameter	IL-8 ≤ 190 pg/ml (n=57)	IL-8 >190pg/ml (n=19)	p-value
Male sex (%)	45 (78.9%)	16 (84.2%)	0.748
Median age (years)†	67 (49-89)	67 (52-79)	0.297
Liver cirrhosis (%)	45 (78.9%)	19 (100%)	0.031
CTP class (%)			
A	40 (88.9%)	15 (78.9%)	0.432
B	5 (11.1%)	4 (21.1%)	
ALBI score†	-2.76 (-3.56 - -1.09)	-2.57 (-3.43 - -1.27)	0.091
ALBI grade*			
1	35 (61.4%)	8 (42.8%)	0.302
2	20 (35.1%)	10 (52.6%)	
3	2 (3.5%)	1 (5.3%)	
MELD score†	6 (6-20)	6 (6-17)	0.186
BCLC stage (%)			
A	0 (0%)	3 (15.8%)	0.022
B	39 (68.4%)	11 (57.9%)	
C	18 (31.6%)	5 (26.3%)	
Portal vein thrombosis (%)	7 (12.3%)	5 (26.3%)	0.161
Macrovascular infiltration (%)	13 (22.8%)	4 (21.1%)	1.000
ALT [IU/L]†	0.55 (0.17-1.67)	0.65 (0.31-1.99)	0.198
AP [IU/L]†	2.35 (0.78-10.89)	2.61 (1.76-5.02)	0.350
GGT [IU/L]†	3.35 (0.86-14.95)	4.01 (0.78-19.68)	0.238
Leucocytes [10 ⁹ /L]†	6.3 (2.3-15.5)	5.6 (3.5-8.8)	0.180
Hemoglobin [gm/dL]†	8.1 (6.3-10.7)	7.7 (4.2-9.7)	0.208
Platelets [10 ⁹ /L]†	138 (40-512)	123 (52-284)	0.389
Albumin [g/L]†	40.2 (27.2-47.0)	38.4 (26.1-47.1)	0.069
Bilirubin [μmol/L]†	12.8 (3.8-43.8)	14.7 (7.8-59.5)	0.330
Creatinine [μmol/L]†	78 (45-211)	77 (50-191)	0.419
AFP [ng/ml]†	28.9 [1.8-60500)	348.5 (2.3-38590)	0.678

†median (range), AFP: alpha-fetoprotein, ALBI: albumin-bilirubin, ALT: alanine aminotransferase, AP: alkaline phosphatase, BCLC: Barcelona Clinic Liver Cancer, CTP: Child-Turcotte-Pugh, GGT: gamma-glutamyl transpeptidase, IL-8: interleukin 8, MELD: model for end-stage liver disease



Supplementary Figure S1. Kaplan-Meier curves are showing the overall survival in patients after TARE of the study cohort (A) and SORAMIC trial (B).