

Supplementary Material

Vascular Complications in Patients with Hepatocellular Carcinoma Treated with Sorafenib

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Table S1. Comparison of baseline characteristics between patients who did versus did not experience thromboembolic complications during sorafenib treatment.

		Without thromboembolic complication (n=244)	With thromboembolic complication (n=8)	p-value
		Number (%) or mean±SD / median (range)		
Age (years)		65±9.5	66±7.7	0.748
Sex	Male	209 (86%)	6 (75%)	0.333
	Female	35 (14%)	2 (25%)	
Etiology	ALD	90 (37%)	3 (38%)	0.160
	Viral	70 (29%)	1 (12%)	
	Unknown	49 (20%)	4 (50%)	
	Other	35 (14%)	-	
Cirrhosis	Yes	182 (75%)	6 (75%)	1.000
Child-Pugh Classification	A	108 (44%)	6 (75%)	0.184
	B	93 (38%)	2 (25%)	
	C	43 (18%)	-	
ECOG PS	0	144 (59%)	5 (63%)	0.898
	≥1	100 (41%)	3 (37%)	
Macrovascular invasion	Yes	118 (48%)	6 (75%)	0.172
Extrahepatic Metastases	Yes	73 (30%)	3 (38%)	0.702
BCLC stage	A	17 (7%)	1 (13%)	0.216
	B	47 (19%)	-	
	C	139 (57%)	7 (87%)	
	D	41 (17%)	-	
Prior therapy	None	137 (56%)	4 (50%)	0.856
	TACE/MWA/RFA	57 (23%)	2 (25%)	
	Resection	11 (5%)	1 (13%)	
	Other	39 (16%)	1 (12%)	
AFP (IU/mL)	Median (range)	50 (0.8-50000)	32 (32-2.5)	0.840
Platelet Count (G/L)	Median (range)	146 (29-778)	237 (115-425)	0.076
Diabetes	Yes	91 (37%)	4 (50%)	0.480
	No	153 (63%)	4 (50%)	
BMI (kg/m²)	Mean±SD	26±5.7	26±4.7	0.908
Obesity (BMI ≥ 30kg/m²)	Yes	56 (23%)	2 (25%)	1.000
Arterial Hypertension	Yes	152 (62%)	2 (25%)	0.057
Antihypertensive treatment	Yes	111 (45%)	1 (12%)	0.079
Smoking	Yes	100 (41%)	6 (75%)	0.072
Hypercholesterinemia (cut-off >200mg/dL)	Yes	53 (22%)	2 (25%)	1.000
Statin therapy	Yes	36 (15%)	2 (25%)	0.346
Hypertriglyceridemia (cut-off >200mg/dL)	Yes	14 (6%)	2 (25%)	0.098

Coronary heart disease	Yes	23 (9%)	-	1.000
Arterial occlusive disease	Yes	20 (8%)	2 (25%)	0.148

Abbreviations: AFP, α -fetoprotein; ALD, alcoholic liver disease; BCLC, Barcelona clinic liver cancer; BMI, Body Mass Index; ECOG PS, Eastern Cooperative Oncology Group performance status; MWA, microwave ablation; RFA, radiofrequency ablation; TACE, transarterial chemoembolization;.

Table S2. Univariate analysis of prognostic factors for overall survival in patients with HCC treated with sorafenib.

		Overall survival (months)			p-value (log rank)
		N	Median	95% CI	
Age	< 65 years	112	10.9	8.6-13.3	0.515
	≥ 65 years	140	8.9	7.1-10.6	
Gender	Male	215	10.2	8.4-12.1	0.237
	Female	37	7.2	4.4-10.1	
Child-Pugh Classification	A	114	13.0	10.5-15.3	0.000
	B	95	7.8	6.0-9.6	
	C	43	4.5	1.2-7.8	
Cardiovascular risk (Framingham risk score)	Low/intermediate	119	10.0	6.8-13.2	0.055
	High	54	7.4	3.4-11.3	
Ascites	No	146	12.5	9.9-15.1	0.000
	Yes	106	6.0	3.7-8.4	
ECOG PS	0	149	11.5	8.0-15.1	0.000
	≥ 1	103	6.6	4.0-9.1	
Macrovascular Invasion	No	125	12.3	9.9-14.7	0.002
	Yes	124	7.3	5.5-9.1	
Extrahepatic spread	No	174	10.0	8.3-11.7	0.722
	Yes	76	7.9	3.5-12.3	
BCLC stage	A	18	13.0	8.6-17.3	0.000
	B	47	12.0	9.9-14.4	
	C	146	9.4	7.4-11.5	
	D	41	4.5	1.3-7.8	
AFP (IU/mL)	≤200	134	10.9	9.1-12.7	0.001
	>200	87	5.4	2.3-8.5	

Abbreviations: AFP, α -fetoprotein; BCLC, Barcelona clinic liver cancer; ECOG PS, Eastern Cooperative Oncology Group performance status.

Table S3. Association of baseline characteristics with the occurrence of bleeding events.

		Without bleeding complication (n=204)	With bleeding complication (n=48)	p-value
		Number (%) or mean±SD / median (range)		
Age (years)		65±9.6	66±8.5	0.875
Sex	Male	172 (84%)	43 (90%)	0.353
	Female	32 (16%)	5 (10%)	
Etiology	ALD	76 (37%)	17 (35%)	0.764
	Viral	55 (27%)	16 (33%)	
	Unknown	45 (22%)	8 (17%)	
	Other	28 (14%)	7 (15%)	
Cirrhosis	Yes	148 (73%)	40 (83%)	0.270
Child-Pugh Classification	A	94 (46%)	20 (42%)	0.718
	B	77 (38%)	18 (37%)	
	C	33 (16%)	10 (21%)	
ECOG PS	0	120 (59%)	29 (60%)	0.973

	≥1	84 (41%)	19 (40%)	
Macrovascular invasion	Yes	101 (50%)	23 (48%)	0.772
Extrahepatic Metastases	Yes	63 (31%)	13 (27%)	0.578
BCLC stage	A	13 (6%)	5 (10%)	0.547
	B	39 (19%)	8 (17%)	
	C	121 (59%)	25 (52%)	
	D	31 (15%)	10 (21%)	
Prior therapy	None	117 (57%)	24 (50%)	0.347
	TACE/MWA/RFA	46 (23%)	13 (27%)	
	Resection	9 (4%)	3 (6%)	
	Other	32 (16%)	8 (17%)	
AFP (IU/mL)	Median (range)	45 (0.8-50000)	108 (1-50000)	0.503
Platelet Count (G/L)	Median (range)	145 (29-778)	154 (47-420)	0.942
Arterial Hypertension	Yes	123 (60%)	31 (65%)	0.636
Antihypertensive treatment	Yes	90 (44%)	22 (46%)	0.830
Smoking	Yes	84 (41%)	22 (46%)	0.557
Coronary heart disease	Yes	20 (10%)	3 (6%)	0.583
Arterial occlusive disease	Yes	19 (9%)	3 (6%)	0.776
Anticoagulation	Yes	27 (13%)	10 (21%)	0.186
Antiplatelet therapy	Yes	33 (16%)	4 (8%)	0.404

Abbreviations: AFP, α -fetoprotein; ALD, alcoholic liver disease; BCLC, Barcelona clinic liver cancer; BMI, Body Mass Index; ECOG PS, Eastern Cooperative Oncology Group performance status; MWA, microwave ablation; RFA, radiofrequency ablation; TACE, transarterial chemoembolization;.

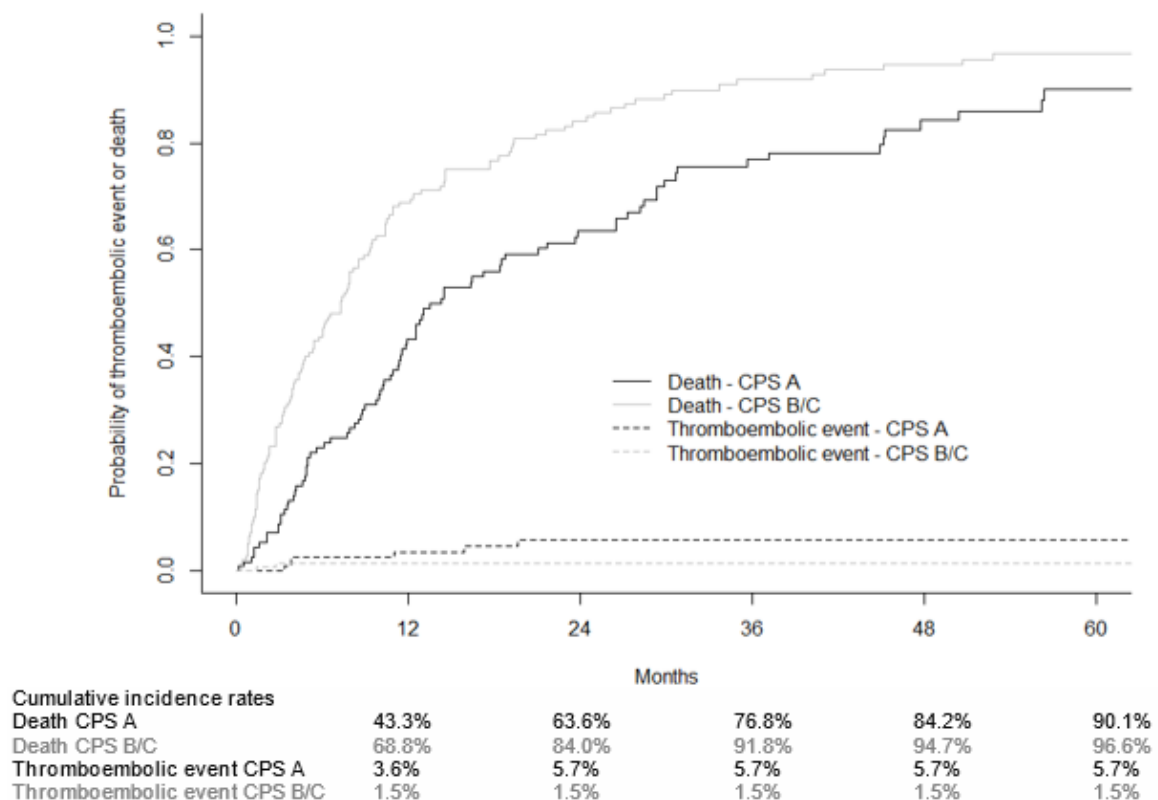


Figure S1. Competing risk analysis comparing the cumulative incidence of thromboembolic events in Child-Pugh A vs. B/C patients. Abbreviations: CPS, Child-Pugh-Score

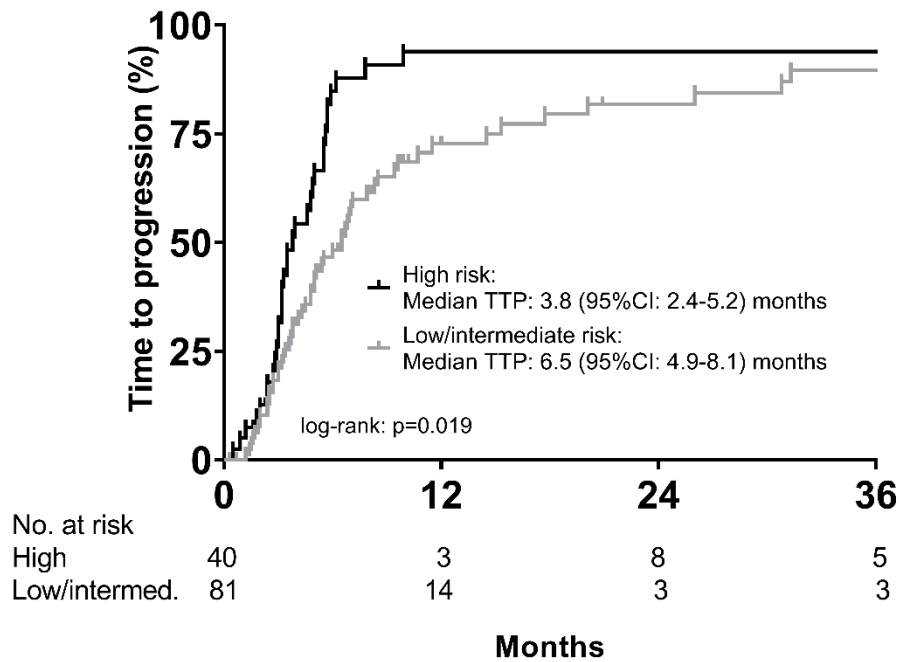


Figure S2. Time to progression (TTP) of patients with low/intermediate risk vs. high risk according to Framingham score. Abbreviations: TTP, time to progression

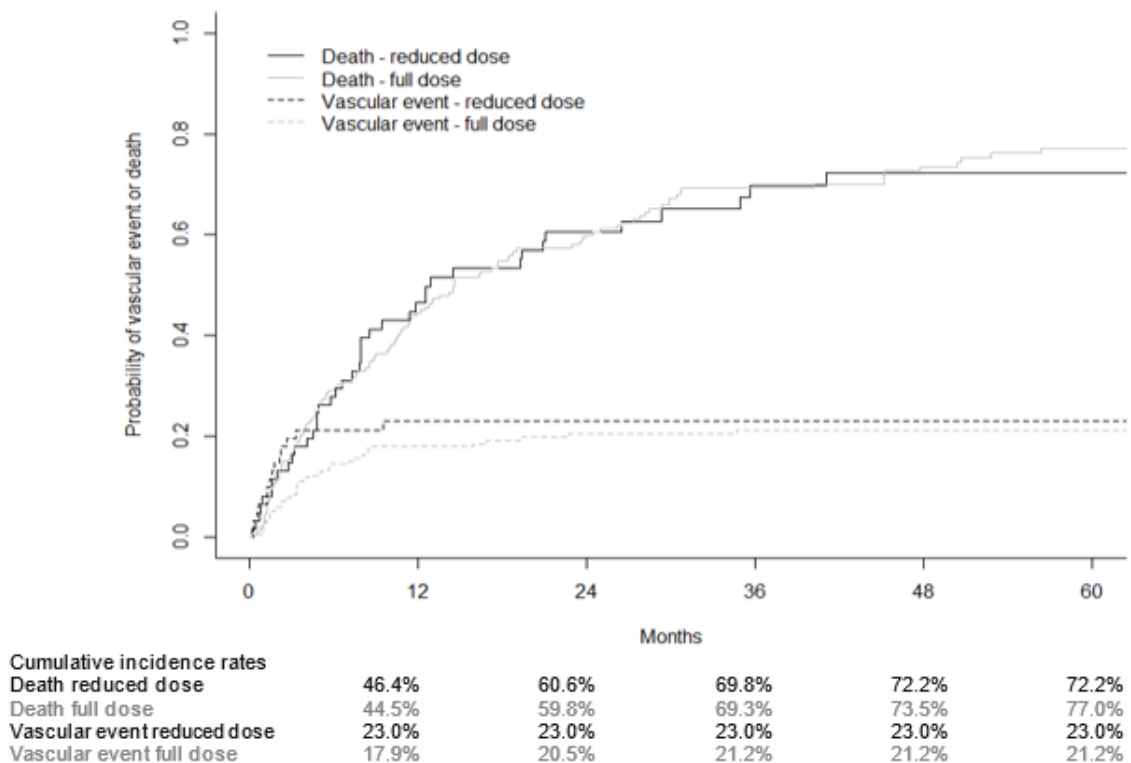


Figure S3. Competing risk analysis of the development of vascular events (thromboembolic and bleeding) with respect to sorafenib starting dose, considering death as competing risk.

