

Supplemental Table 1. Characteristics of patients included vs. excluded from the primary study cohort

Variable	Included patients (n = 242)	Excluded patients* (n = 1804)	p-value
Age, years (SD)	60.3 (7.9)	61.1 (9.8)	0.20
Sex (% male)	210 (87.1)	1409 (78.2)	0.001
Race/Ethnicity			0.31
White	119 (49.2)	838 (46.5)	
Black	70 (28.9)	468 (25.9)	
Hispanic	38 (15.7)	338 (18.7)	
Asian	6 (2.5)	76 (4.2)	
Other/Unknown	9 (3.7)	84 (4.7)	
Cirrhosis etiology			0.001
Hepatitis C	169 (69.8)	1097 (60.8)	
Alcohol-related	36 (14.9)	210 (11.6)	
NAFLD	16 (6.6)	253 (14.0)	
Hepatitis B	8 (3.3)	104 (5.8)	
Other	8 (3.3)	43 (2.4)	
Unknown/None	5 (2.1)	97 (5.4)	
Child Pugh Class			0.78
A	121 (51.3)	967 (53.7)	
B	89 (37.7)	646 (35.9)	
C	26 (11.0)	187 (10.4)	
AFP, ng/mL			<0.001
< 20	127 (52.4)	737 (40.8)	
20 – 199	62 (25.6)	426 (23.7)	
>200	30 (12.4)	547 (30.3)	
Missing	23 (9.6)	94 (5.2)	
Largest initial tumor diameter, cm	2.6 (1.9 – 3.9)	3.9 (2.4 – 8.0)	<0.001
Number lesions			<0.001
1	166 (68.6)	945 (52.4)	
2	54 (22.3)	330 (18.3)	
3 or more	22 (9.1)	529 (29.3)	

Within Milan (%)	178 (73.6)	869 (48.2)	<0.001
First HCC treatment			<0.001
Resection	25 (10.3)	274 (15.2)	
Ablation	31 (12.8)	227 (12.6)	
OLT	22 (9.1)	36 (2.0)	
TACE/TARE	82 (33.9)	597 (33.1)	
SBRT	14 (5.8)	47 (2.6)	
Systemic therapy	10 (4.1)	172 (9.5)	
None/BSC	58 (24.0)	451 (25.0)	

*Data provided as median (IQR) or n (%) except where otherwise specified

* Data from subset (61.4%) of excluded patients with available data

Supplemental Table 2. Specific growth rate (SGR) and tumor doubling time (TDT) measurements in patient subgroups[#]

	SGR (% per day)	TDT (days)
Initial tumor diameter		
1-2 cm	0.38 (0.14 – 0.95)	182 (73 – 495)
2-5 cm	0.32 (0.11 – 0.78)	217 (89 – 630)
>5 cm	0.17 (0.06 – 0.46)	408 (151 – 1155)
Cirrhosis etiology		
Viral	0.34 (0.13 – 0.80)	204 (87 – 533)
Non-viral	0.19 (0.06 – 0.59)	365 (117 – 1155)

[#]Results for primary cohort

Supplemental Table 3. Correlates of rapid HCC growth patterns*#

Variable	Univariable Analysis		Multivariable Analysis	
	OR	95% CI	OR	95% CI
Age	0.99	0.96 – 1.02		
Male sex	0.97	0.50 – 1.91		
BMI				
Normal	Ref	Ref		
Overweight	0.85	0.50 – 1.46		
Obese	0.71	0.39 – 1.29		
NLR	1.03	0.92 – 1.15		
Race/ethnicity				
White	Ref	Ref		
Black	0.97	0.56 – 1.67		
Hispanic	0.87	0.44 – 1.72		
Asian	0.94	0.22 – 4.04		
Child Pugh class				
A	Ref	Ref		
B	1.11	0.67 – 1.84		
C	0.91	0.43 – 1.92		
AFP > 20	1.65	1.04 – 2.65	1.65	1.02 – 2.68
Initial tumor diameter (continuous)	0.87	0.78 – 0.98	0.86	0.77 – 0.97
Etiology				
Viral	Ref	Ref	Ref	Ref
Non-viral	0.60	0.35 – 1.02	0.67	0.38 – 1.17

*Results from ordinal logistic regression model comparing indolent vs. intermediate vs. rapid tumor growth patterns, respectively.

#Results for primary cohort

Supplemental Table 4. Correlates of specific growth rate (SGR) #

Variable	Univariable Analysis		Multivariable Analysis	
	Coeff.	95% CI	Coeff.	95% CI
Age	.00002	-.0001 - .0001		
Male sex	.0013	-.0015 - .0041		
BMI	-.0002	-.0003 - .00002	-.0001	-.0003 - .00004
NLR	-4.05*10 ⁶	-.0005 - .0005		
Race/ethnicity				
White	Ref	Ref		
Non-white	.0001	-.0018 - .0019		
Etiology				
Viral	Ref	Ref		
Non-viral	-.0016	-.0037 - .0005		
Child Pugh class				
A	Ref	Ref		
B	.0007	-.0013 - .0028		
C	-.0003	-.0032 - .0027		
AFP > 20	.0028	.0010 - .0047	.0029	.0010-.0048
AFP > 500	.0001	-.0023 - .0026		
AFP > 1000	.0009	-.0017 - .0036		
Initial tumor diameter	-.0005	-.0009 - -.0001	-.0006	-.0010- -.0001
Initial tumor count > 1	-.0014	-.0034 - .0006		

#Results for primary cohort

AFP – alpha-fetoprotein; BMI – body mass index; CI – confidence interval; NLR – neutrophil-lymphocyte ratio

Supplemental Table 5. Characteristics of patients in the primary study cohort who underwent treatment vs those who remained untreated (n=242)

Variable	Treated patients (n = 184)	Untreated patients (n = 58)	p-value
Age, years (SD)	61.6 (7.0)	56.1 (9.2)	<0.001
Sex (% male)	162 (88.5)	48 (82.8)	0.25
Race/Ethnicity			0.002
White	99 (53.8)	20 (34.5)	
Black	55 (29.9)	15 (25.9)	
Hispanic	20 (10.9)	18 (31.0)	
Asian	4 (2.2)	2 (3.5)	
Other/Unknown	6 (3.2)	3 (5.1)	
Cirrhosis etiology			0.19
Hepatitis C	128 (69.6)	41 (70.7)	
Alcohol-related	23 (12.5)	13 (22.4)	
NAFLD	15 (8.2)	1 (1.7)	
Hepatitis B	6 (3.3)	2 (3.5)	
Other	7 (3.8)	1 (1.7)	
Unknown/None	5 (2.6)	0 (0.0)	
Child Pugh Class			<0.001
A	99 (55.0)	22 (39.3)	
B	71 (39.4)	18 (32.1)	
C	10 (5.6)	16 (28.6)	
AFP, ng/mL			0.80
< 20	96 (52.2)	31 (53.4)	
20 – 199	47 (25.5)	15 (25.9)	
>200	21 (11.4)	9 (15.5)	
Missing	20 (10.9)	3 (5.2)	
Largest initial tumor diameter, cm	2.5 (1.8 – 3.8)	2.9 (2.0 – 4.4)	0.22
Number lesions			0.02
1	130 (70.6)	36 (62.1)	
2	34 (18.5)	20 (34.5)	
3 or more	20 (10.8)	2 (3.4)	

Within Milan (%)	142 (77.2)	36 (62.1)	0.02
------------------	------------	-----------	------

*Data provided as median (IQR) or n (%) except where otherwise specified