

Comparing the Prognostic Value of Quantitative Response Assessment Tools and LIRADS Treatment Response Algorithm in Patients with Hepatocellular Carcinoma Following Interstitial High Dose Rate Brachytherapy and Conventional Transarterial Chemoembolization

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Supplementary Material

Supplement Table S1. Survival measures comparing patients stratified as non-responders vs. responders following interstitial brachytherapy (iBT).

iBT		Survival measures in months for non-responders vs. responders, median [IQR]						
Time	Criterion	OS	PFS	PFS _{LTP}	PFS _{IDR}	TTP	TTP _{LTP}	TTP _{IDR}
2 Months	RECIST	22.3 [14.2,46.9]	9.6 [4.9,15.7]	14.6 [8.3,48.1]	11.6 [5.5,16.5]	9.6 [5.4,32.7]	59.8 [14.6,n/d]	12.2 [8.2,44.8]
		vs. 26.4 [15.4,37.4]	vs. 6.4 [5.1,7.0]	vs. 11.1 [5.1,46.0]	vs. 7.0 [5.8,7.0]	vs. 9.4 [5.1,10.3]	vs. n/d [n/d,n/d]	vs. 13.0 [5.5,10.3]
	WHO	36.3 [15.1,63.8]	10.9 [5.1,16.5]	14.6 [8.3,48.1]	13.0 [5.8,15.4]	9.6 [5.1,21.6]	n/d [9.1,n/d]	13.0 [8.3,39.7]
		vs. 15.1 [12.2,41.7]	vs. 5.4 [4.9,15.4]	vs. 13.7 [11.1,41.7]	vs. 9.2 [8.3,22.7]	vs. 8.2 [4.9,18.4]	vs. n/d [35.2,n/d]	vs. 12.2 [5.8,18.4]
	mRECIST	36.3 [12.8,55.6]	10.9 [2.1,39.7]	13.1 [10.7,55.6]	10.9 [2.1,39.7]	6.5 [2.1,39.7]	n/d [n/d,n/d]	6.5 [2.1,39.7]
		vs. 26.3 [15.0,45.2]	vs. 9.1 [5.0,15.0]	vs. 14.6 [7.4,41.7]	vs. 12.7 [7.3,15.7]	vs. 9.4 [5.1,18.8]	vs. n/d [9.1,n/d]	vs. 14.8 [8.3,31.6]

5 Months	EASL	25.8 [12.8,55.6] vs. 26.3 [15.0,45.3]	7.4 [2.1,13.1] vs. 9.1 [5.1,15.4]	13.0 [10.7,55.6] vs. 14.6 [8.6,42.7]	9.6 [2.1,11.6] vs. 13.0 [8.3,16.5]	6.7 [11.6,2.1] vs. 11.0 [5.4,18.8]	n/d [n/d,n/d] vs. n/d [9.1,n/d]	8.2 [2.1,11.6] vs. 15.3 [8.6,32.7]
	LI-TRA v2018	15.2 [12.8,61.1] vs. 29.6 [15.7,45.2]	16.2 [13.1,63.1] vs. 8.6 [4.9,14.6]	13.1 [7.4,61.1] vs. 15.0 [8.6,42.7]	11.6 [7.0,14.6] vs. 13.0 [7.3,22.7]	11.0 [5.5,21.6] vs. 8.6 [4.9,18.8]	n/d [9.1,n/d] vs. n/d [35.2,n/d]	11.8 [9.6,21.6] vs. 13.0 [5.8,36.4]
	LI-TRA v2024	26.4 [13.3,62.1] vs. 30.1 [15.9,45.9]	11.1 [5.6,14.9] vs. 8.7 [4.7,15.9]	14.1 [11.1,62.1] vs. 15.2 [8.4,42.4]	11.8 [2.4,18.4] vs. 13.3 [5.1,20.1]	11.1 [5.6,21.9] vs. 9.3 [4.9,19.1]	n/d [n/d,n/d] vs. n/d [8.7,n/d]	11.9 [8.4,40.4] vs. 13.2 [5.9,33.2]
	RECIST	21.8 [14.6,45.2] vs. 49.8 [15.2,63.8]	8.3 [4.7,14.8] vs. 12.1 [9.6,63.2]	14.0 [7.0,41.7] vs. 39.2 [12.8,63.2]	12.2 [9.8,14.9] vs. 12.1 [5.9,23.1]	8.3 [5.1,21.6] vs. 15.0 [9.6,63.2]	n/d [8.3,n/d] vs. n/d [8.6,n/d]	12.2 [7.3,31.6] vs. 18.4 [9.6, n/d]
	WHO	33.2 [15.0,45.3] vs. 22.9 [15.2,62.3]	11.0 [8.6,21.9] vs. 8.3 [4.9,15.4]	14.0 [8.3,42.7] vs. 16.9 [12.8,62.3]	14.0 [7.3,21.6] vs. 10.3 [8.3,62.3]	8.3 [5.0,21.6] vs. 10.9 [8.3,18.4]	n/d [8.3,n/d] vs. n/d [35.2,n/d]	14.8 [5.8,32.7] vs. 10.9 [8.3, 18.4]
	mRECIST	31.6 [15.0,45.2] vs. 23.8 [14.6,45.3]	5.3 [4.9,13.1] vs. 11.0 [7.0,15.4]	14.1 [6.3,45.2] vs. 14.6 [8.3,42.7]	7.3 [5.5,14.8] vs. 13.0 [8.6,21.6]	5.5 [5.0,11.6] vs. 11.0 [8.3,21.6]	n/d [6.3,n/d] vs. n/d [15.0,n/d]	6.6 [5.5,14.8] vs. 15.4 [9.4, 32.7]
	EASL	28.9 [15.0,45.2] vs. 26.3 [14.6,63.2]	5.1 [2.1,4.9] vs. 11.1 [8.3,16.5]	12.7 [6.3,45.2] vs. 15.0 [8.6,63.2]	6.6 [5.5,12.2] vs. 14.0 [8.6,2.7]	5.3 [4.9,5.8] vs. 13.0 [8.3,21.6]	n/d [5.1,n/d] vs. n/d [15.0,n/d]	5.8 [5.4,12.2] vs. 15.4 [9.4,36.4]
	LI-TRA v2018	36.6 [15.0,63.8] vs. 22.9 [14.6,45.2]	8.3 [2.6,14.8] vs. 11.0 [5.1,15.4]	13.0 [5.1,61.1] vs. 15.1 [10.7,45.2]	11.6 [7.0,22.3] vs. 14.0 [7.3,22.7]	9.6 [2.6,14.8] vs. 9.4 [5.5,18.8]	n/d [4.7,n/d] vs. n/d [15.0,n/d]	11.8 [9.6,21.6] vs. 15.3 [7.3,36.4]
	LI-TRA v2024	31.8 [14.6,62.1] vs.	10.4 [4.7,15.0] vs.	13.2 [7.1,62.1] vs.	11.8 [7.1,15.0] vs.	11.7 [4.7,15.0] vs.	n/d [5.2,n/d] vs.	12.4 [7.4,36.9] vs.

	27.7 [15.3,64.9]	8.7 [5.1,15.6]	15.4 [8.7,45.9]	13.2 [7.4,23.1]	8.7 [5.5,19.1]	n/d [15.2,n/d]	13.2 [9.8,21.9]
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OS overall survival, PFS progression-free survival, TTP time-to-progression, LTP local tumor progression subtype, IDR intrahepatic distant recurrence subtype, RECIST Response Evaluation Criteria in Solid Tumors v1.1, mRECIST modified RECIST, WHO World Health Organization, EASL European Study of the Liver, LI-TRA Liver Imaging and Reporting Data System (LIRADS) Treatment Response Algorithm, n/d non-defined. Data is depicted as median and interquartile range (IQR).

Supplement Table S2. Survival measures comparing patients stratified as non-responders vs. responders following conventional chemoembolization (cTACE)/interstitial brachytherapy (iBT).

cTACE/iBT		Survival measures in months for Non-Responders vs. Responders, median [IQR]						
Time	Criterion	OS	PFS	PFS _{LTP}	PFS _{IDR}	TTP	TTP _{LTP}	TTP _{IDR}
2 Months	RECIST	24.0 [15.1,48.0] vs. 11.0 [8.1,13.8]	7.6 [2.5,19.4] vs. 9.1 [5.2,12.9]	20.1 [9.2,29.1] vs. 9.1 [5.2,12.9]	7.9 [2.6,19.8] vs. 9.6 [6.3,12.9]	7.9 [2.6,19.6] vs. 12.9 [5.2,27.4]	n/d [25.6,n/d] vs. 12.9 [5.2,n/d]	11.9 [4.7,19.9] vs. 27.4 [6.3,27.4]
	WHO	24.7 [6.0,48.0] vs. 6.9 [5.8,13.0]	8.4 [2.6,19.6] vs. 4.7 [4.2,7.9]	21.1 [9.9,38.3] vs. 7.5 [5.2,13.0]	11.9 [3.2,19.8] vs. 6.3 [4.2,7.9]	9.1 [2.6,19.6] vs. 7.9 [5.2,27.4]	n/d [20.7,n/d] vs. n/d [26.4,n/d]	12.0 [4.7,19.9] vs. 7.9 [6.3,27.4]
	mRECIST	18.2 [8.7,48.0] vs. 23.3 [15.1,47.6]	2.3 [1.9,5.2] vs. 11.3 [5.2,19.6]	17.9 [5.3,38.3] vs. 21.4 [9.9,26.6]	2.3 [1.9,6.3] vs. 13.2 [7.6,19.9]	2.4 [2.1,7.5] vs. 11.9 [6.1,19.8]	n/d [24.1,n/d] vs. n/d [n/d,n/d]	2.4 [2.1,7.5] vs. 18.1 [7.9,27.4]
	EASL	18.2 [8.7,51.9] vs. 23.3 [15.1,44.3]	2.3 [1.9,5.2] vs. 11.0 [5.2,19.6]	17.9 [5.3,38.3] vs. 21.4 [9.9,26.4]	2.3 [1.9,6.3] vs. 13.2 [7.5,19.9]	2.4 [2.1,11.3] vs. 11.9 [6.1,19.8]	n/d [20.7,n/d] vs. n/d [24.1,n/d]	2.4 [2.1,11.3] vs. 18.1 [7.6,27.4]
	LI-TRA v2018	22.0 [15.6,38.8] vs. 23.1 [13.8,64.6]	6.4 [2.5,20.7] vs. 7.8 [3.2,19.4]	18.5 [8.7,26.4] vs. 20.4 [9.7,47.6]	6.9 [2.5,20.9] vs. 12.4 [5.0,19.6]	7.5 [2.5,20.7] vs. 9.1 [4.8,19.6]	26.4 [20.7,n/d] vs. n/d [24.1,n/d]	7.5 [2.5,20.9] vs. 12.4 [5.1,19.9]
	LI-TRA v2024	21.1 [8.8,30.9] vs. 23.5 [14.0,65.7]	5.2 [2.3,18.3] vs. 8.6 [3.2,19.7]	18.4 [5.9,26.0] vs. 20.8 [9.8,65.7]	5.8 [2.4,18.4] vs. 13.1 [5.1,20.1]	11.2 [4.7,21.0] vs. 7.7 [2.3,19.9]	26.9 [21.0,n/d] vs. n/d [24.5,n/d]	12.6 [4.7,23.0] vs. 8.0 [2.3,20.1]

5 Months	RECIST	24.7 [17.3,47.6] vs. 51.9 [26.6,64.7]	7.6 [4.2,19.6] vs. 11.3 [9.2,12.9]	21.1 [11.0,38.3] vs. 26.4 [9.2,26.5]	7.9 [4.7,19.9] vs. 12.9 [11.3,47.6]	7.6 [4.7,19.8] vs. 11.3 [9.2,18.1]	n/d [24.1,n/d] vs. 26.5 [12.9,n/d]	12.0 [5.0,19.9] vs. 18.1 [10.6,27.4]
	WHO	27.7 [17.9,48.0] vs. 21.6 [13.8,26.6]	7.6 [4.2,19.6] vs. 12.9 [7.9,18.1]	21.1 [9.9,38.3] vs. 21.6 [13.0,26.4]	11.3 [4.7,20.9] vs. 12.9 [7.9,18.1]	7.6 [4.7,19.6] vs. 12.9 [7.9,19.9]	n/d [24.1,n/d] vs. n/d [26.4,n/d]	12.0 [5.0,20.9] vs. 18.1 [6.3,27.4]
	mRECIST	19.8 [15.6,38.8] vs. 28.8 [19.4,65.0]	5.1 [4.7,7.5] vs. 11.9 [6.9,19.6]	18.1 [9.9,25.6] vs. 24.7 [13.0,26.5]	5.1 [4.7,7.5] vs. 14.0 [7.6,19.9]	5.0 [4.7,6.1] vs. 12.4 [7.9,19.8]	n/d [20.7,n/d] vs. n/d [26.4,n/d]	5.1 [4.7,7.5] vs. 18.1 [10.6,27.4]
	EASL	19.8 [15.6,30.4] vs. 28.8 [19.4,51.9]	5.1 [4.7,6.1] vs. 11.9 [6.9,19.8]	18.1 [9.9,25.6] vs. 24.4 [13.0,44.3]	5.1 [4.7,7.5] vs. 14.0 [6.9,19.9]	5.0 [4.7,6.1] vs. 12.4 [7.6,19.9]	n/d [25.6,n/d] vs. n/d [24.1,n/d]	5.1 [4.7,6.1] vs. 18.1 [7.9,27.4]
	LI-TRA v2018	18.2 [9.7,26.6] vs. 31.6 [17.3,62.7]	5.0 [2.6,18.1] vs. 10.1 [5.2,19.6]	17.9 [5.2,20.7] vs. 24.4 [11.0,62.7]	5.0 [2.6,18.1] vs. 13.2 [9.2,26.5]	5.2 [2.6,20.7] vs. 10.8 [5.1,19.6]	25.6 [20.7,26.4] vs. n/d [26.5,n/d]	6.3 [2.6,20.9] vs. 13.2 [6.9,27.4]
	LI-TRA v2024	18.5 [15.8,39.0] vs. 28.9 [19.7,65.7]	4.7 [2.6,21.3] vs. 9.3 [5.3,19.7]	18.2 [9.8,25.1] vs. 25.8 [13.1,48.4]	4.7 [2.6,23.3] vs. 13.3 [6.4,20.0]	5.1 [2.6,21.3] vs. 10.1 [5.3,19.9]	n/d [21.0,n/d] vs. n/d [24.5,n/d]	5.1 [2.6,23.0] vs. 12.6 [6.4,20.1]

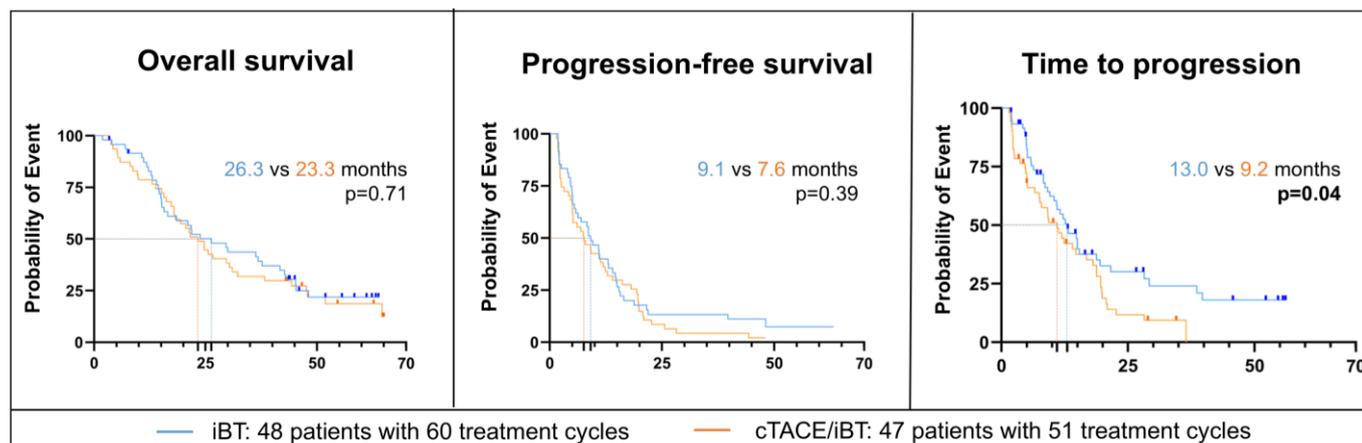
OS overall survival, PFS progression-free survival, TTP time-to-progression, LTP local tumor progression subtype, IDR intrahepatic distant recurrence subtype, RECIST Response Evaluation Criteria in Solid Tumors v1.1, mRECIST modified RECIST, WHO World Health Organization, EASL European Study of the Liver, LI-TRA Liver Imaging and Reporting Data System (LIRADS) Treatment Response Algorithm, n/d non-defined. Data is depicted as median and interquartile range (IQR).

Supplement Table S3. Uni- and multivariate cox proportional hazard model results.

	OS			PFS			TTP		
	95% CI (exp B)	HR	p- value	95% CI (exp B)	HR	p- value	95% CI (exp B)	HR	p- value
Univariate analysis									

iBT vs. cTACE/iBT	0.61-1.48	0.95	0.81	0.84-1.85	1.25	0.27	0.89-2.11	1.38	0.15
age	0.98-1.00	0.98	0.07	0.98-1.02	1.00	0.99	0.97-1.02	0.99	0.56
male vs. female sex	0.47-1.36	0.80	0.41	0.65-1.71	1.05	0.84	0.54-1.50	0.90	0.69
lesions	0.87-1.34	1.08	0.50	0.93-1.50	1.18	0.18	0.79-1.41	1.05	0.72
sum of lesion diameter	1.00-1.02	1.01	0.02	0.99-1.01	1.00	0.79	0.99-1.01	1.00	0.95
non-viral vs. viral cause of cirrhosis	0.56-1.53	0.92	0.76	0.55-1.36	0.86	0.53	0.59-1.56	0.96	0.87
Child Pugh class A vs. B	1.25-5.28	2.57	0.01	0.69-2.80	1.39	0.35	0.57-2.75	1.25	0.58
BCLC stage A vs. B	0.89-2.51	1.50	0.13	0.68-1.78	1.10	0.70	0.57-1.69	0.98	0.93
BCLC stage A vs. C	0.90-3.66	1.81	0.09	0.89-3.3	1.71	0.11	0.91-1.95	1.82	0.09
Alpha-fetoprotein (AFP)	0.99-1.00	1.00	0.28	1.00-1.00	1.00	0.33	1.00-1.00	1.00	0.31
ALBI score	1.65-4.74	2.79	<0.01	0.93-2.44	1.51	0.09	0.67-1.95	1.14	0.62
AST/ALT-ratio	0.84-1.69	1.19	0.32	0.72-1.62	1.08	0.72	0.61-1.53	0.97	0.88
Multivariate analysis									
age	0.95-1.01	0.98	0.29						
sum of lesion diameter	0.99-1.02	1.01	0.08						
Child Pugh class A vs. B	0.22-2.65	0.76	0.67						
BCLC stage A vs. C	0.70-4.50	1.77	0.23						
ALBI score	1.38-7.73	3.25	<0.01						

OS, overall survival; PFS, progression-free survival; TTP, time to progression; CI, confidence intervals; HR, hazard ratio; iBT, interstitial high dose-rate brachytherapy; cTACE, conventional transarterial chemoembolization.



Supplement Figure S1. Overall survival (OS), progression-free survival (PFS) and time to progression (TTP) in patients following interstitial brachytherapy (iBT, blue line) alone or with a combined prior conventional transarterial chemoembolization (cTACE/iBT, orange). Dashed lines show 95% confidence intervals. Kaplan-Meier analyses reveal no significant differences for OS and PFS, but for TTP.

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