

Background

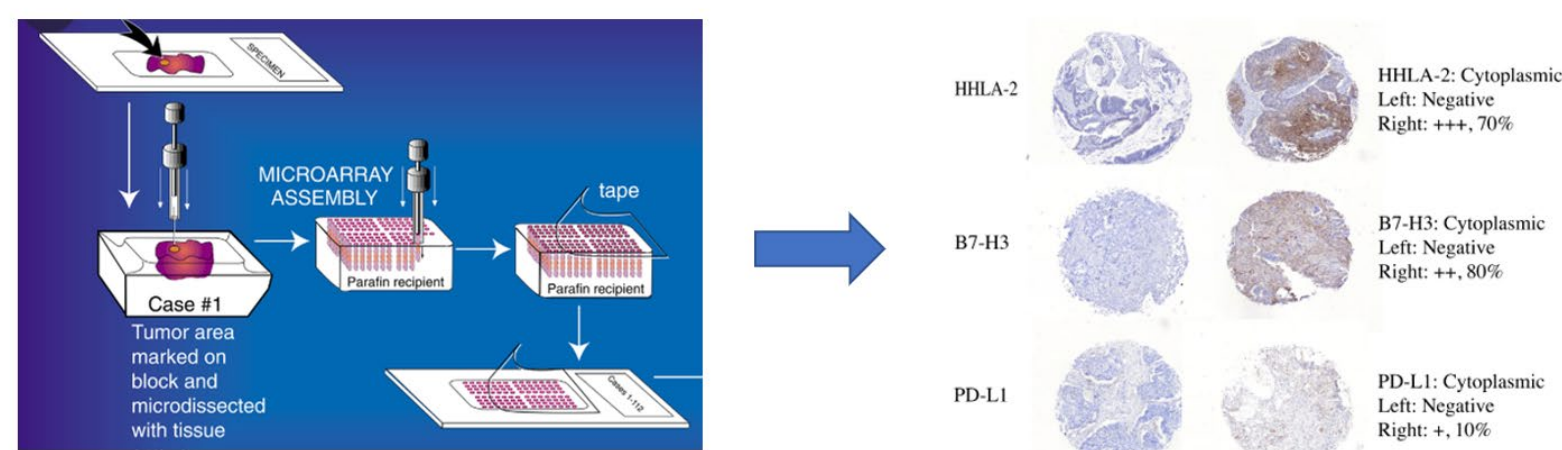
Immunotherapy has emerged as an effective and durable treatment modality for solid cancers. However, its use in colorectal cancer (CRC) is limited to deficient mismatch repair (dMMR) tumors. As such, assessing immune regulatory proteins from the B7-CD28 family, other than PD-1, PD-L1, and CTLA-4, is critical. This study aimed to compare the median overall survival of patients with metastatic CRC by B7H3 expression. in a racially diverse population of patients with CRC.

Objectives

- To compare the median overall survival of patients with mCRC by B7H3 expression.
- To identify prognostic factors in a multiracial cohort of patients with mCRC.

Methods

A tumor microarray was created for 200 samples from a multiracial patient population with metastatic CRC, and expression of HHLA2, B7-H3 and PD-L1 was determined. The expression pattern was scored as 0 to 12, based on tumor tissue prevalence and the intensity.



Clinical information was obtained by chart review and vital statistics from the National Death Index. Clinical and pathological factors were compared between B7H3 expression groups. Clinically meaningful variables and variables that Attained a p-value < 10.10 in univariate analysis were included in a multivariate Cox Proportional Hazards Model. Kaplan-Meier curves were plotted, and log-rank tests were performed to test the difference in overall survival among low and high B7H3 expression groups.

The mean age at diagnosis was 60.5 years, with a female predominance. Most of the patients were diagnosed with de novo metastatic disease with left-sided, moderately differentiated tumors.

There were no racial disparities in the expression of any protein. Overall, a high frequency of tumors had no expression of B7-H3 (62.5%) or PD-L1 (43.5%).

Low expression of both PD-L1 and B7-H3 was a significant prognostic biomarker associated with better survival (median overall survival, 43.3 months vs. 24.6 months; P < .01).

Table 1: Baseline characteristics by B7H3 expression

	All n=200	B7H3 Low Expressors n=125	B7H3 High Expressors n=75	p
Mean age (SD)	60.5 (13.4)	60.2 (13.7)	61 (12.9)	0.67
Gender				0.63
-Male	81 (40.5)	49 (39.2)	32 (42.7)	
-Female	119 (59.5)	76 (60.8)	43 (57.3)	
Race/Ethnicity				0.12
-Non-Hispanic White	36 (18)	21 (16.8)	15 (20)	
-Non-Hispanic Black	85 (42.5)	61 (48.8)	24 (32)	
-Hispanic	76 (38)	41 (32.8)	35 (46.7)	
-Asian	3 (1.5)	2 (1.6)	1 (1.3)	
Marital status*				0.98
-Married	64 (32.3)	40 (32.3)	24 (32.4)	
-Other	134 (67.7)	84 (67.7)	50 (67.6)	
Sidedness+				0.59
-Right	51 (33.3)	29 (30.5)	22 (37.9)	
-Transverse	15 (9.8)	9 (9.5)	6 (10.3)	
-Left	87 (56.9)	57 (60)	30 (51.7)	
Presentation				0.21
-De novo	125 (62.5)	74 (59.2)	51 (68)	
-Recurrent	75 (37.5)	51 (40.8)	24 (32)	

Results are presented as n (%), unless otherwise specified.
SD: standard deviation.
*Data was missing in 2 participants.
+Data was missing in 47 participants.

Results

Table 2: Pathologic characteristics by B7H3 expression

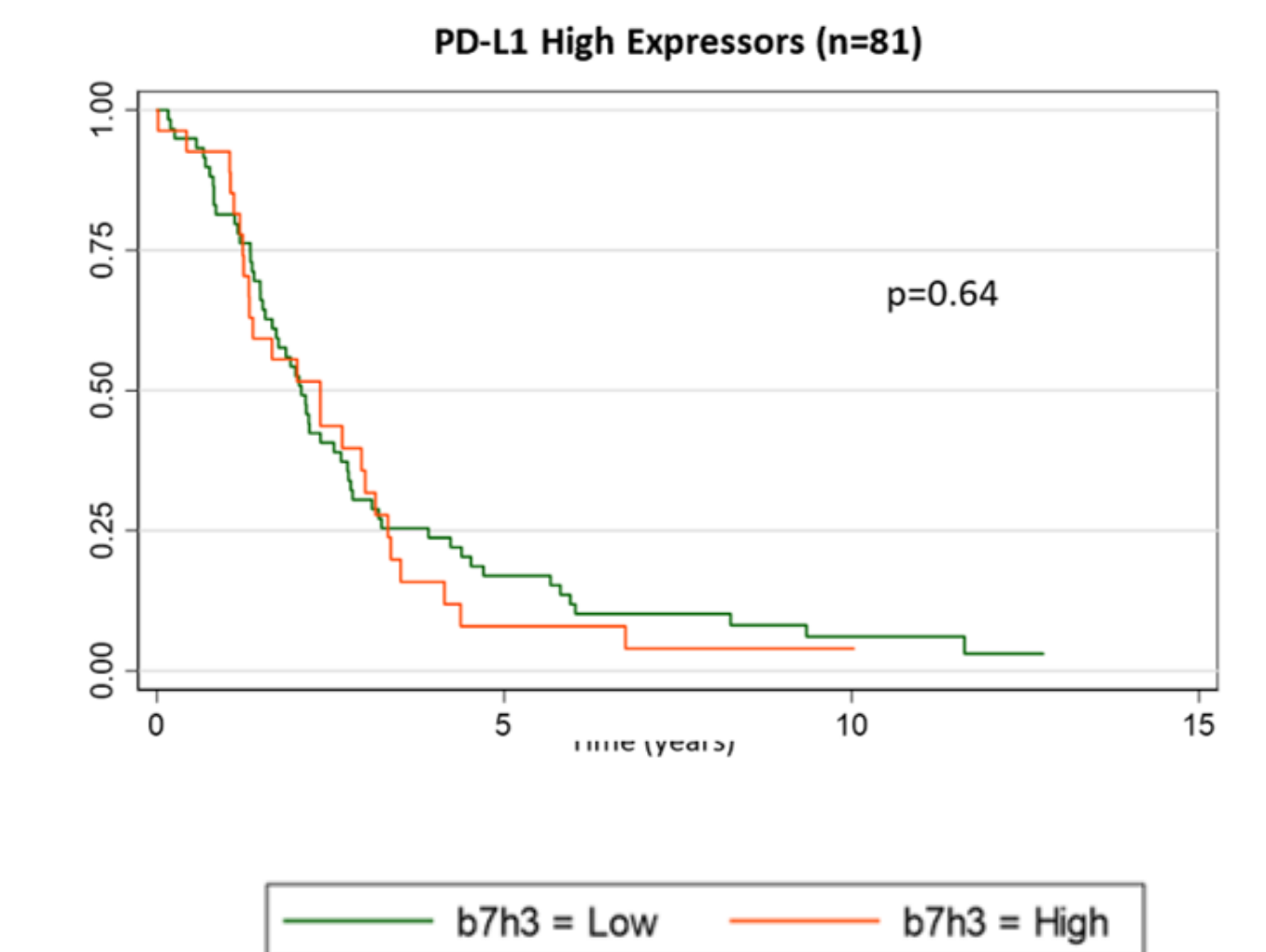
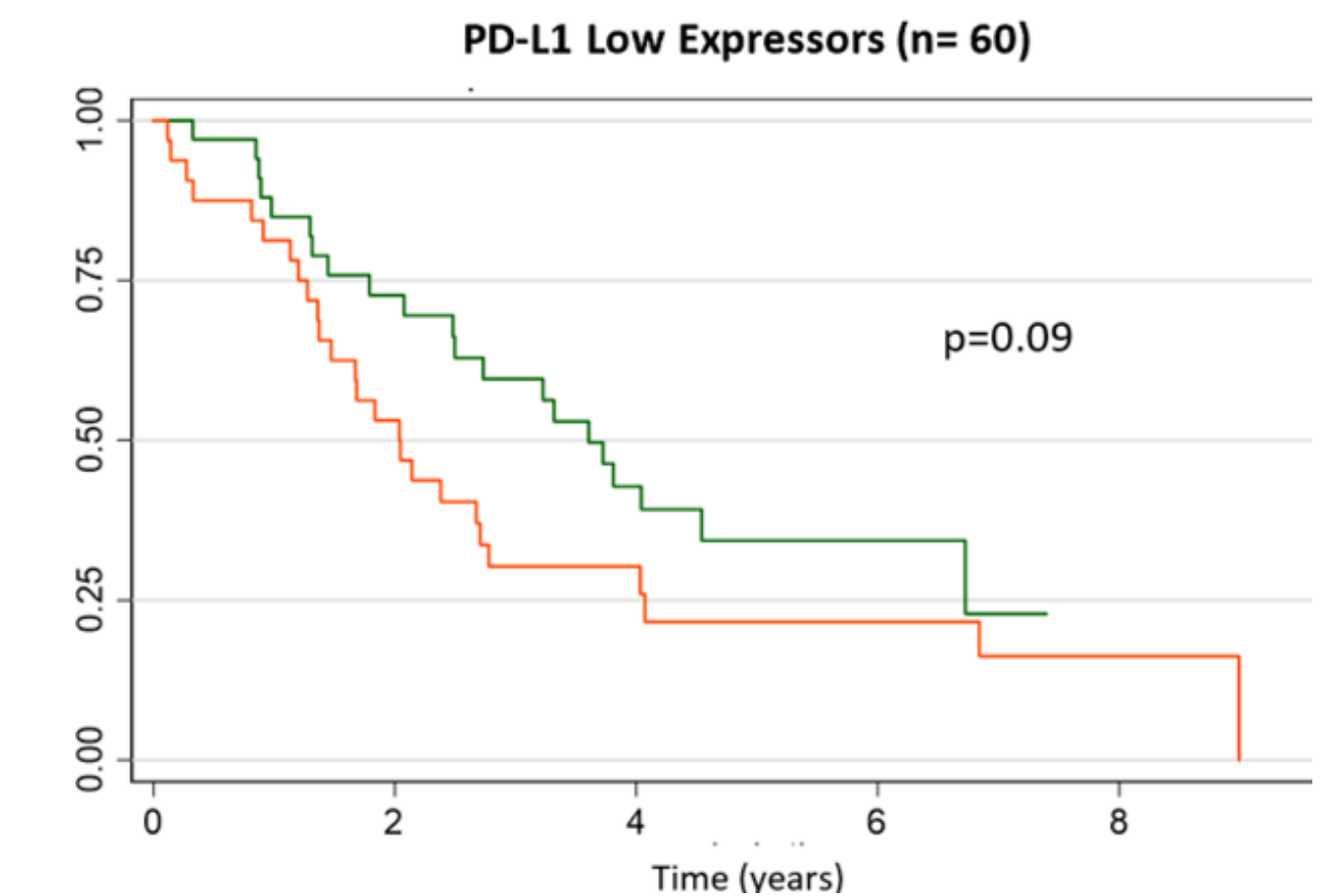
	All n=200	B7H3 Low Expressors n=125	B7H3 High Expressors n=75	p
Grade*				0.14
-Well	14 (12.4)	14 (11.5)	10 (13.9)	
-Moderate	122 (62.9)	83 (68)	39 (54.2)	
-Poor	48 (24.7)	25 (20.5)	23 (31.9)	
T Stage*				0.13
-T1-3	92 (65.7)	60 (70.6)	32 (58.2)	
-T4	48 (34.3)	25 (29.4)	23 (41.8)	
N Stage [†]				<0.01
-N0	35 (25.7)	24 (29.3)	11 (20.4)	
-N1	54 (39.7)	38 (46.3)	16 (29.6)	
-N2	47 (34.6)	20 (24.4)	27 (50)	
PD-L1				0.03
-Low	66 (43.4)	34 (36.6)	32 (54.2)	
-High	86 (56.6)	59 (63.4)	27 (45.8)	
HHLA2				0.59
-Low	120 (61.8)	76 (63.3)	44 (59.5)	
-High	74 (38.2)	44 (36.7)	30 (40.5)	

Results are presented as n (%), unless otherwise specified.
T: Tumor, N: Lymph Node
*Data was missing in 16 participants.
+Data was missing in 60 participants.
†Data was missing in 64 participants.

Table 3: Cox Proportional Model Stratified by PD-L1 expression

	PD-L1 Low Expressors (n=61)			PD-L1 High Expressors (n=81)		
	HR	95% CI	p	HR	95% CI	p
B7H3						
-Low	1			1		
-High	3.02	1.39 - 6.55	<0.01	0.77	0.44-1.35	0.37
Age	1.02	1.01 - 1.05	0.04	1.01	0.98 - 1.03	0.42
Gender						
-Male	1			1		
-Female	0.48	0.23 - 0.99	0.05	0.85	0.50 - 1.44	0.56
Race/Ethnicity						
-Non-Hispanic White	1			1		
-Non-Hispanic Black	0.90	0.32 - 2.48	0.83	1.63	0.83 - 3.18	0.15
-Hispanic	0.89	0.34 - 2.33	0.82	1.79	0.88 - 3.65	0.11
-Asian	0.44	0.05 - 3.86	0.46			
Sidedness						
-Right-sided	1			1		
-Transverse	0.83	0.27 - 2.60	0.76	0.46	0.19 - 1.19	0.11
-Left-sided	0.26	0.13 - 0.55	<0.01	0.51	0.19 - 0.85	0.01

HR: Hazard-ratio, CI: Confidence Interval.



Conclusion

- In a model adjusted for age, gender, race/ethnicity and sidedness; B7H3 was found to be a prognostic factor in patients with low PD-L1 expression. The risk of mortality is three times higher in those with high B7H3 expression compared to those with low B7H3 expression in this group.