Comparison of Tumor Immune Microenvironments (TIMEs) Between Primary and Metastatic Sites (Mets) in Triple Negative Breast Cancer (TNBC)

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INTRODUCTION

The TIME is critical in determining response to immune checkpoint inhibitors (ICIs), but TIME differences across primary and mets in TNBC are not well understood. Since ICIs are standard of care for patients with TNBC, we studied the TIMEs of primary TNBC and mets to investigate how immune composition may affect ICI efficacy across different met sites. Secondary analysis stratified cohorts by race and disease sites to compare TIMEs in Black or African American (B/AA) with White patients, since TNBC has a high prevalence of B/AA women who are underrepresented in studies and have a worse prognosis.

METHODS

N=1,044 de-identified patient records of TNBC were selected from the Tempus Database. Tumors from primary breast (PB), liver, lymph node (LN), lung, and bone sites were sequenced with the Tempus xT DNA (648-gene panel) and xR RNA assays.

Demographics, TMB, MSI, PD-L1, and proportions of B, T (CD4+, CD8+), NK cells, and macrophages were compared across sites. LN were used as a positive control. Chi-squared/Fisher's exact or Kruskal-Wallis tests were used to assess statistical significance (two-sided, evaluated at the 0.05 alpha level).

Patient Characteristics

Characteristic	Overall N=1,044[1]	PB n=553[1]	Liver n=153[1]	LN n=174[1]	Lung n=111[1]	Bone n=53[1]	p-value[2]
Age at Diagnosis							0.022
Age at Diagnosis, Median (IQR)	57 (46, 66)	58 (46, 68)	57 (47, 65)	56 (48, 66)	53 (44, 62)	64 (49, 71)	
Gender							0.3
Female	1,040 (100%)	550 (99%)	153 (100%)	174 (100%)	111 (100%)	52 (98%)	
Race							0.5
White	457 (65%)	236 (61%)	66 (68%)	78 (66%)	50 (74%)	27 (82%)	
Black or African American	160 (23%)	96 (25%)	22 (23%)	27 (23%)	12 (18%)	3 (9%)	
Other	85 (12%)	53 (14%)	9 (9%)	14 (11%)	6 (8%)	3 (9%)	
Smoker status							0.007
Never smoker	486 (60%)	273 (62%)	68 (61%)	88 (67%)	36 (42%)	21 (55%)	
Current/former smoker	324 (40%)	170 (38%)	44 (39%)	44 (33%)	49 (58%)	17 (45%)	

[1]n (%)
[2]Kruskal-Wallis rank sum test; Fisher's Exact Test for Count Data with simulated p-value (based on 2000 replicates)

Table 1. The cohort (median age=57 years, IQR 46-66) comprised a diverse population (65% White, 23% B/AA, 2.8% Asian, and 9.3% other). PD-L1 positivity, TMB, and MSI exhibited no differences across sites. Percentages are calculated from known data.

SUMMARY

- Compared to primary breast and lung, liver and bone had immune cell infiltrates indicating a less immunogenic TIME in the overall TNBC population.
- Although limited by sample size, this is one of the first studies to assess the TIME across race and sites of disease.
- These findings are hypothesis generating and provide further rationale to better understand how the TIME across disease sites and race may alter the efficacy of ICIs in TNBC.

RESULTS

Immune Infiltration by Metastatic Sites Across the Cohort

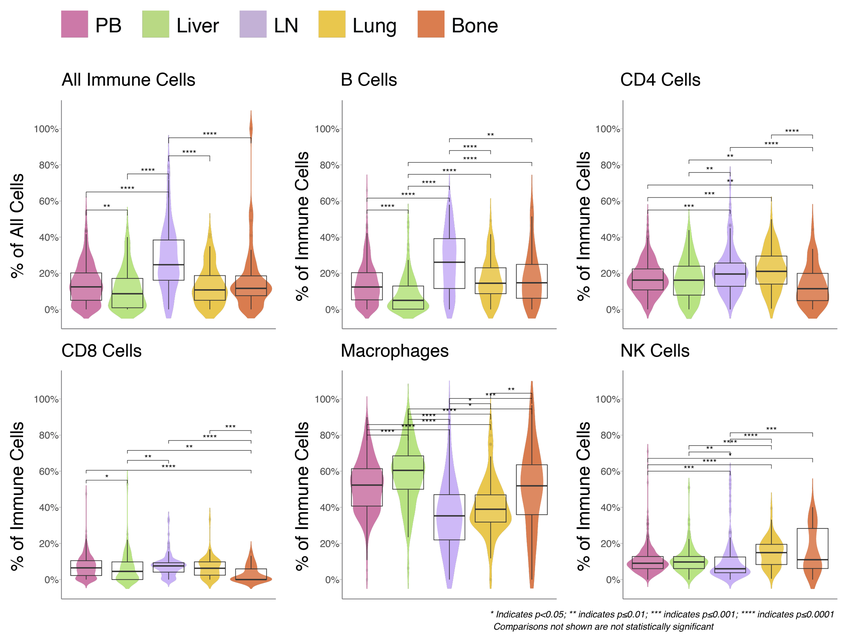

Figure 1. Liver exhibited a lower percentage of B cells and higher percentage of macrophages compared to PB (p<0.0001 for both), lung (p<0.0001 for both), and bone (B cells p<0.0001, macrophages p<0.05). Liver also exhibited lower percentages of CD8+ T cells compared to PB (p<0.05) and CD4+ and NK cells compared to lung (CD4+ cells p<0.01, NK cells p<0.0001). Bone had lower percentages of CD8+ cells compared to PB (p<0.0001), lung (p<0.001), and liver (p<0.01). Compared to lung, bone had a lower percentage of CD4+ cells (p<0.0001) and higher percentage of macrophages (p<0.01).

Immune Infiltration by Metastatic Sites in B/AA Compared with White Patients

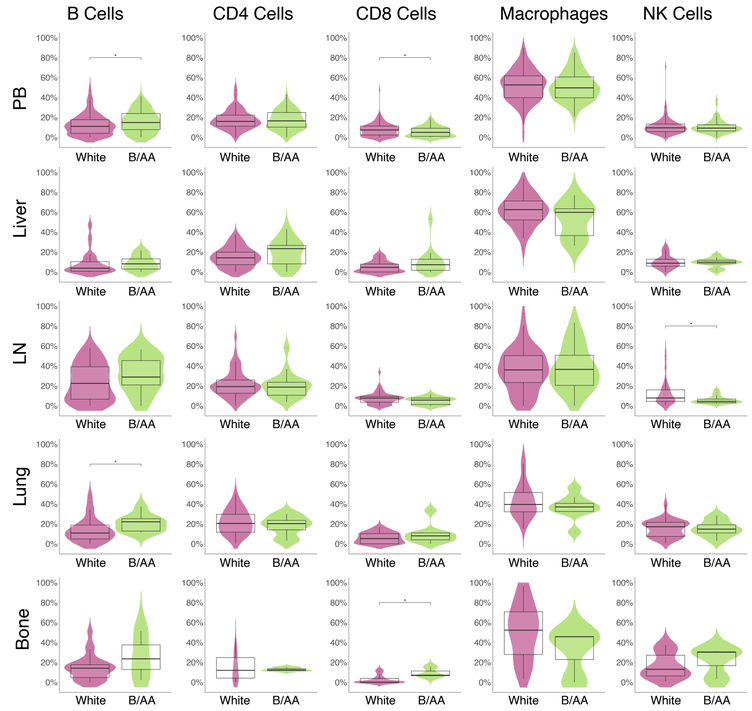

Figure 2. Secondary analysis compared the TIME between B/AA and White cohorts in PB (B/AA n=85 vs White n=204: %B cells, 15 vs 11, p=0.017; %CD8 cells, 4.9 vs 7.3, p=0.025), liver (B/AA n=15 vs White n=48: %B cells, 8 vs 4, p=0.2; %CD4, 23 vs 14, p=0.2; %CD8, 7.2 vs 4.6, p=0.07), and lung (B/AA n=9 vs White n=33: %B cells, 22 vs 11, p=0.021; %CD8, 7.9 vs 5.2, p=0.5).

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