San Antonio Breast Cancer Symposium® - December 10 -13, 2024

Characterization of the Tumor Immune Microenvironment (TIME) and Somatic Landscape of Metaplastic Breast Cancer (MpBC)

Shaveta Vinayak[1,2], Lynn Symonds[1,2], Eric Konnick[1,2], Natasha Hunter[1,2], William Gwin[1,2], Denise Shieh[3], Matina Fragkogianni[3], Michelle Harris[3], Jacob Mercer[3], Hannah Linden[1,2], Jennifer Specht[1,2]

[1]University of Washington, Seattle, WA, [2] Fred Hutchinson Cancer Center, Seattle, WA, [3]Tempus AI, Inc, Chicago, IL, USA

INTRODUCTION

- Metaplastic Breast Cancer (MpBC) is a rare and aggressive subtype with poor prognosis and limited treatment options, necessitating novel therapies.
- Recent studies show immune checkpoint inhibitors can be effective.
- Understanding the immune and genomic environments in MpBC is crucial for developing new biomarker-based strategies.
- This study examines the TIME and somatic landscape of MpBC.

METHODS

- Next-generation sequencing data from 13,510 pts with breast cancer in the Tempus database, including 171 with MpBC (1.3%) and 13,339 with non-MpBC (98.7%), were analyzed based on clinical documentation within 180 days of sample collection, with one sample per patient.
- The cohorts were racially diverse with no significant difference (p=0.5).
- Sequencing was performed using Tempus xT DNA (648-gene panel) and/or xR RNA assays to evaluate somatic mutations, immune cell (% of total cells) infiltration, TMB, and MSI. PD-L1 expression was analyzed by IHC (CPS, 22C3).
- Statistical significance was determined using Wilcoxon rank-sum and Pearson's Chi-squared/Fisher's exact tests, with a significance threshold of p<0.05 and q<0.05.

Acknowledgements: We thank Amrita A. Iyer, PhD for assistance with poster preparation.

Correspondence: shaveta@uw.edu

KEY TAKEAWAYS

- In this large, real-world analysis, tumors from patients with MpBC displayed a distinct molecular phenotype compared to tumors from patients with non-MpBC. In tumors from patients with MpBC, TNBC was more common, whereas the HER2+ subtype was rare.
- Tumors from patients with MpBC had higher PD-L1 expression and therapeutically relevant alterations, including those within the PI3k pathway, were frequently encountered.
- Although limited by sample size, this is one of the first studies to compare the molecular phenotypes between subtypes within tumors from patients with MpBC.
- These findings are hypothesis-generating and provide further rationale for developing novel combinatorial therapeutic clinical trial strategies for patients with MpBC.

RESULTS

Patient cohort characteristics

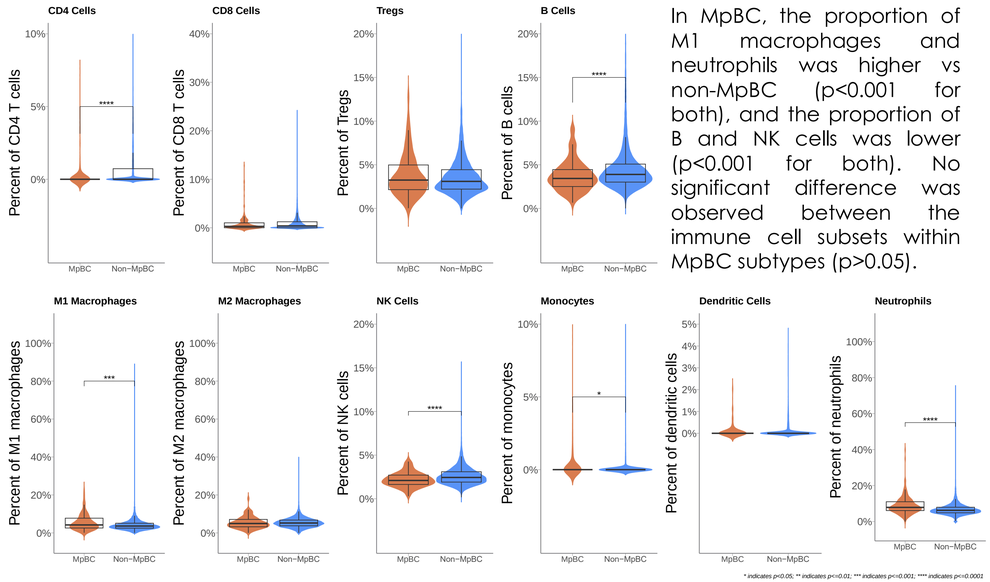
Characteristic	Overall N = 13,510[1]	MpBC N = 171[1]	Non-MpBC N = 13,339[1]	p-value[2]
Age at primary diagnosis				<0.0001
Median (IQR)	57 (47,66)	61 (50,72)	57 (47,66)	
Range	19, 90	28, 88	19, 90	
Unknown	69	0	69	
Gender				0.3
Female	13,346 (99%)	171 (100%)	13,175 (99%)	
Male	158 (1.2%)	0 (0%)	158 (1.2%)	
Unknown	6	0	6	
Race				0.5
White	6,468 (73%)	82 (72%)	6,386 (73%)	
Black/African American	1,298 (15%)	14 (12%)	1,284 (15%)	
Asian	392 (4.4%)	9 (7.9%)	383 (4.4%)	
American Indian/Alaska Native	43 (0.5%)	0 (0%)	43 (0.5%)	
Native Hawaiian/other Pacific Islander	15 (0.2%)	0 (0%)	15 (0.2%)	
Other	619 (7.0%)	9 (7.9%)	610 (7.0%)	
Unknown	4,675	57	4,618	
Ethnicity				0.7
Not Hispanic or Latino	4,988 (86%)	57 (88%)	4,931 (86%)	
Hispanic or Latino	799 (14%)	8 (12%)	791 (14%)	
Unknown	7,723	106	7,617	
HR/HER2 Status closest to sample collection				<0.001
HR+, HER2-	7,419 (63%)	33 (22%)	7,386 (63%)	
TNBC	3,212 (27%)	116 (76%)	3,096 (27%)	
HER2+	1,173 (9.9%)	3 (2.0%)	1,170 (10%)	
Unknown	1,706	19	1,687	

[1]n(%), [2]Wilcoxon rank sum test, Fisher's exact test, Pearson's chi-square test

Immune biomarkers:

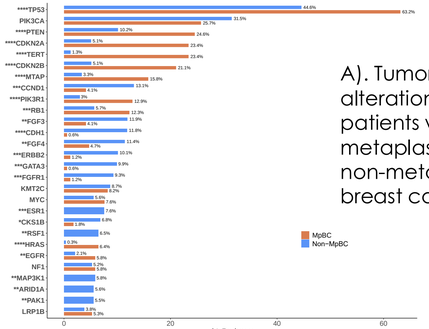
- PD-L1 expression (CPS ≥ 10)
  - MpBC (35%) vs non-MpBC (14%) (p<0.001).
  - MpBC cohort: PD-L1 expression (CPS ≥ 10) in TNBC (38%) and HR+/HER2- (33%)(p>0.5).
- TMB and MSI: No clinically significant difference in overall and metaplastic-specific analysis (p>0.05 for both)

Immune infiltration by cell type

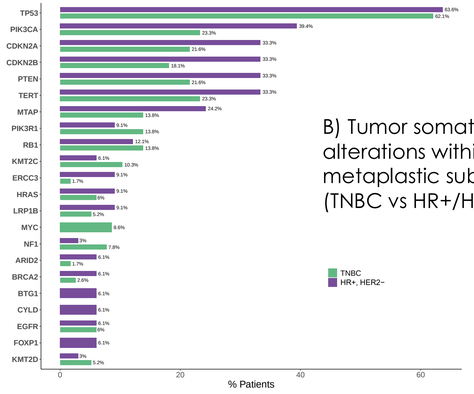


In MpBC, the proportion of M1 macrophages and neutrophils was higher vs non-MpBC (p<0.001 for both), and the proportion of B and NK cells was lower (p<0.001 for both). No significant difference was observed between the immune cell subsets within MpBC subtypes (p>0.05).

Somatic landscape in patients with MpBC and non-MpBC



A). Tumor somatic alterations between patients with metaplastic and non-metaplastic breast cancer.



B) Tumor somatic alterations within the metaplastic subtypes (TNBC vs HR+/HER2-)