Circulating Immune Correlates of Pathological Response to Neoadjuvant Pembrolizumab plus Chemotherapy in High-Risk, Early-Stage Triple-Negative Breast Cancer

Clinton Yam[1], Anastasia Radko[2], Lei Huo[3], Akshara Singareeka[1], Elina Ohanjanyan[2], Anastasiya Yudina[4], Vladimir Kushnarev[5], Holly Hill[6], Sausan Abouharb[1], Beatriz Adrada[7], Banu Arun[1], Carlos Barcenas[1], Ajit Bisen[1], Abenaa Brewster[1], Aman Buzdar[1], Mariana Chavez Mac Gregor[1], Senthil Damodaran[1], Haven Garber[1], Mary Guirguis[7], Amy Hassan[1], Nuhad Ibrahim[1], Meghan Karuturi[1], Elisabeth Kong[8], Rachel Layman[1], Giancarlo Moscol[1], Jason Mouabbi[1], Rashmi Murthy[1], Azadeh Nasrazadani[1], Blessie Nelson[1], Adaeze Nwosu Iheme[1], Oluchi Oke[1], Miral Patel[7], Paula Pohlmann[1], David Ramirez[1], Sadia Saleem[1], Jasmine Sukumar[1], Jia Sun[9], Parijatham Thomas[1], Ronald Walters[1], Peng Wei[9], Madison Williams[1], Matthew Wright[1], Wendy A. Woodward[10], Kelly K. Hunt[11], Jennifer K. Litton[1], Vicente Valero[1], Debu Tripathy[1], Gaiane Rauch[7], Michael Goldberg[12], Anil Korkut[13].

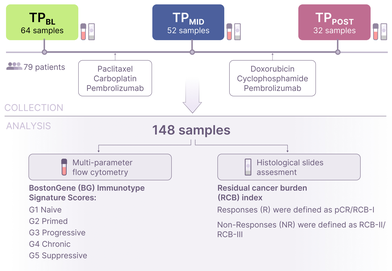
1 — Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; 2 — Immunoprofiliing Research and Development, BostonGene Corporation, Waltham, MA; 3 — Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX; 4 — Engineering, BostonGene Corporation, Waltham, MA; 5 — Research Project Management, BostonGene Corporation, Waltham, MA; 6 — Precision Oncology Decision Support, The University of Texas MD Anderson Cancer Center, Houston, TX; 7 — Breast Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX; 8 — Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX; 9 — Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; 10 — Breast Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; 11 — Breast Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; 12 — Research and Development, BostonGene Corporation, Waltham, MA; 13 — Bioinformatics and Computational Biology, The University of Texas MD Anderson Cancer Center, Houston, TX.

Background

- Pembrolizumab (anti-PD-1) has been incorporated into neoadjuvant therapy for stage II-III triple-negative breast cancer and has improved patient outcomes.
- Despite these advances, immune-related adverse events remain a clinical concern.
- Therefore, there is a critical need to identify patients most likely to benefit from this regimen.
- We report circulating immune biomarkers associated with pathological response in patients treated with neoadjuvant pembrolizumab plus chemotherapy (KEYNOTE-522 regimen) enrolled onto the prospective ARTEMIS trial (NCT02276443).

Methods

Patients with stage II-III TNBC planned to receive the KEYNOTE-522 regimen were enrolled on the prospective ARTEMIS trial (NCT02276443).



Results

Table 1. Baseline clinicopathological characteristics.

	All (N=79)	Responder (R, N=59)	Non-Responder (NR, N=15)	P value
Age at diagnosis	51.0 (40.7-59.9)	48.9 (39.4-59.9)	52.5 (45.1-66.9)	52.5 (45.1-66.9)
Race				
White	41 (59.5)	33 (56)	12 (80)	ref
Black	12 (15.2)	10 (17)	1 (7)	0.24
Hispanic or Latino	17 (21.5)	14 (24)	1 (7)	0.14
Asian	3 (3.8)	2 (3)	1 (7)	0.80
Histology				
Ductal	69 (87.3)	54 (92)	12 (80)	ref
Metaplastic	5 (6.3)	2 (3)	1 (7)	0.52
Other	4 (5.1)	3 (6)	1 (7)	0.74
Missing	1 (1.3)	0	1 (7)	
Histologic grade				
2	12 (15)	9 (15)	2 (13)	ref
3	66 (84)	50 (85)	12 (80)	0.93
missing	1 (1)	0	1 (7)	
T stage				
T1	18 (23)	13 (22)	5 (33)	ref
T2	46 (58)	37 (63)	7 (47)	0.29
T3	8 (10)	5 (8)	2 (13)	0.97
T4	7 (9)	4 (7)	1 (7)	0.73
Nodal status				
Negative	51 (65)	39 (66)	7 (47)	ref
Positive	51 (65)	20 (34)	8 (53)	0.17

Figure 1. Immunotype heatmap at baseline (TP_{BL}).

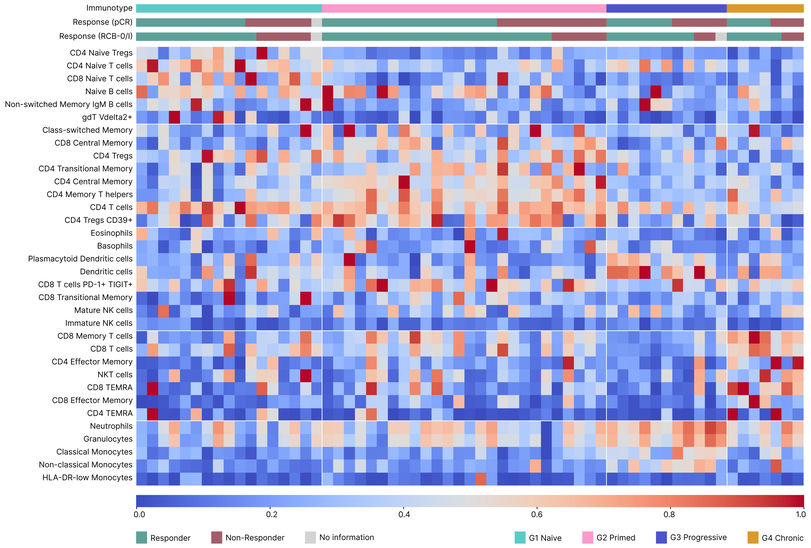


Figure 2. Cell percentages in R vs NR at baseline.

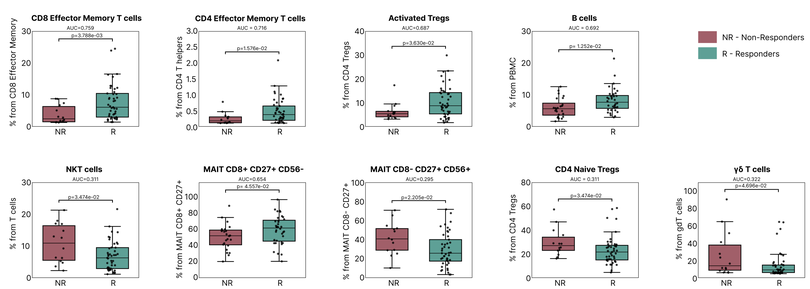


Figure 3. Major immune cell population dynamics.

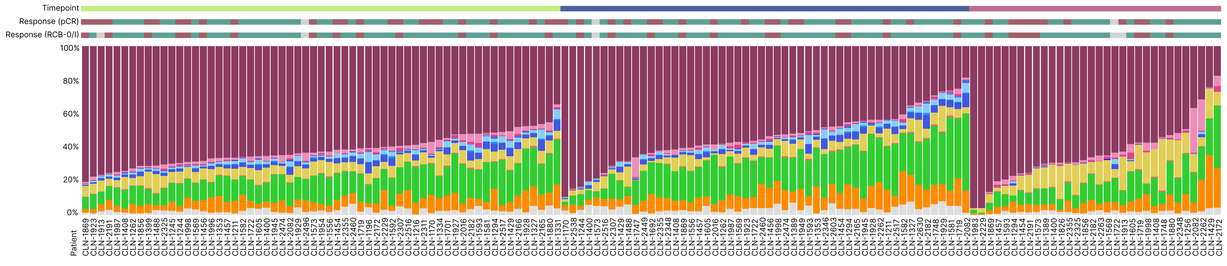


Figure 4. Immune cell populations at TP_{BL}, TP_{MID}, TP_{POST}.

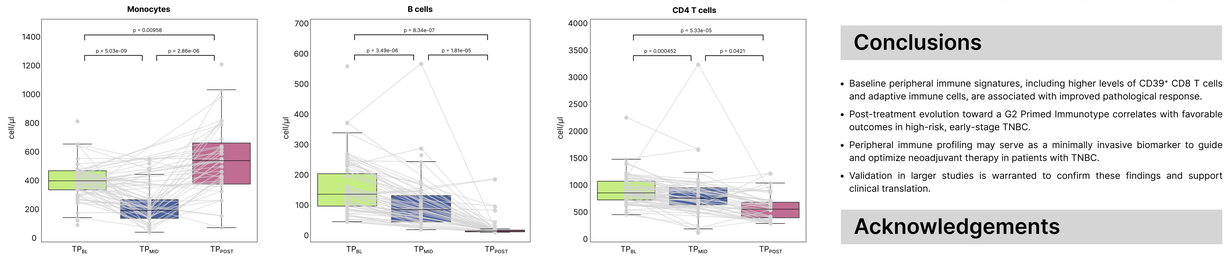
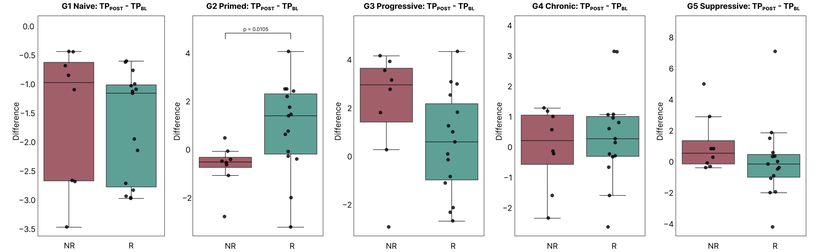


Figure 5. Immunotype dynamics in R vs NR across the 3 timepoints.



Conclusions

- Baseline peripheral immune signatures, including higher levels of CD39⁺ CD8 T cells and adaptive immune cells, are associated with improved pathological response.
- Post-treatment evolution toward a G2 Primed Immunotype correlates with favorable outcomes in high-risk, early-stage TNBC.
- Peripheral immune profiling may serve as a minimally invasive biomarker to guide and optimize neoadjuvant therapy in patients with TNBC.
- Validation in larger studies is warranted to confirm these findings and support clinical translation.

Acknowledgements

The authors wish to express their heartfelt thanks to:
BostonGene Corporation for research funding and research analytical support;
Conquer Cancer, the ASCO Foundation for research funding;
The University of Texas **MD Anderson Cancer Center** Breast Cancer Moon Shot Program for research funding and infrastructure;
Stillwater Foundation for research funding;
Most importantly, our patients who have courageously volunteered for this study.

References

Schmid, Peter, et al. "Pembrolizumab for early triple-negative breast cancer." New England Journal of Medicine 382.9 (2020): 810-821.

Schmid, Peter, et al. "Event-free survival with pembrolizumab in early triple-negative breast cancer." New England Journal of Medicine 386.6 (2022): 556-567.

Pusztai, L., et al. "Event-free survival by residual cancer burden with pembrolizumab in early-stage TNBC: exploratory analysis from KEYNOTE-522." Annals of Oncology 35.5 (2024): 429-436.

Dent, Rebecca, et al. "Neoadjuvant pembrolizumab plus chemotherapy/adjuvant pembrolizumab for early-stage triple-negative breast cancer: quality-of-life results from the randomized KEYNOTE-522 study." JNCI: Journal of the National Cancer Institute 116.10 (2024): 1654-1663.

Contact: Clinton Yam cyam@mdanderson.org