Racial/Ethnic Differences in Site of Metastasis at Presentation and Treatment in *de novo* Metastatic Triple-Negative Breast cancer

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Background

Triple-negative breast cancer (TNBC) is an aggressive disease that disproportionately affects Black and Hispanic patients in the U.S.

Racial/ethnic minority patients are diagnosed at younger ages, later stages, face barriers in accessing oncology care, and overall experience worse outcomes, despite improvements in early detection and treatment.

There remains limited data on racial/ethnic and socioeconomic disparities in pattern of metastatic disease at presentation, treatment receipt, and initiation in metastatic TNBC nationally.

Methods and Materials

Using the National Cancer Database (NCDB), we analyzed a retrospective cohort of patients diagnosed with *de novo* metastatic TNBC between 2010 and 2022.

We evaluated 3 metastatic sites, including brain, bone only, and visceral (liver and/or lung).

Three treatment modalities were assessed: immunotherapy (IO), chemotherapy (chemo), and radiotherapy (RT).

- IO use was restricted to patients treated with chemo from 2019 to 2022, following the initial accelerated FDA approvals for atezolizumab in 2019 and pembrolizumab in 2020 for PD-L1+ metastatic TNBC.

Treatment initiation delay (i.e., number of days) was defined as the time from initial diagnosis to treatment start and compared by site of metastasis across racial/ethnic groups.

Multiple linear regression was used to examine racial/ethnic differences in treatment initiation delay, adjusting for clinicopathologic and socioeconomic factors. Regression coefficients (β) and 95% CIs were calculated.

Results

Of 16,897 patients included, the mean age was 61.6 (SD, 14.2) years; 62.9% were White, 26.3% Black, 6.9% Hispanic, 2.9% Asian or Pacific Islander (API), and 1.0% Other (per self-report)

12.0%, 24.5%, and 57.4% had brain, bone only, and visceral metastases at presentation, respectively; 55.8% received chemo alone, 44.2% IO, and 31.8% RT as their first line of treatment.

Table 1. Distributions of Time to Treatment Initiation for *de novo* Metastatic TNBC by Race/Ethnicity

	White	Black	API	Hispanic	Other	*P*
No. of days between diagnosis and chemo start						
Mean (SD)	42.9 (36.4)	47.1 (45.1)	41.0 (36.7)	51.2 (61.8)	54.8 (47.7)	<.001
Median (IQR)	34.0 (22.0, 52.0)	39.0 (24.0, 58.0)	33.0 (20.0, 51.0)	40.0 (25.0, 62.0)	41.0 (26.0, 68.0)	<.001
No. of days between diagnosis and IO start						
Mean (SD)	68.1 (63.2)	74.3 (70.4)	61.6 (46.2)	82.7 (78.7)	106.1 (153.7))	.003
Median (IQR)	50.0 (33.0, 80.0)	56.0 (37.0, 82.0)	48.0 (32.0, 73.0)	53.0 (37.0, 97.0)	57.0 (41.0, 101.0)	.020
No. of days between diagnosis and RT start						
Mean (SD)	118.2 (115.8)	138.9 (125.5)	150.6 (128.9)	158.6 (121.5)	139.5 (153.6)	<.001
Median (IQR)	65.0 (24.0, 211.0)	92.0 (30.0, 242.0)	105.0 (33.0, 259.0)	137.5 (48.0, 256.5)	91.0 (28.0, 237.0)	<.001

Figure 1. Metastatic Sites at Presentation in *de novo* TNBC by Race/Ethnicity

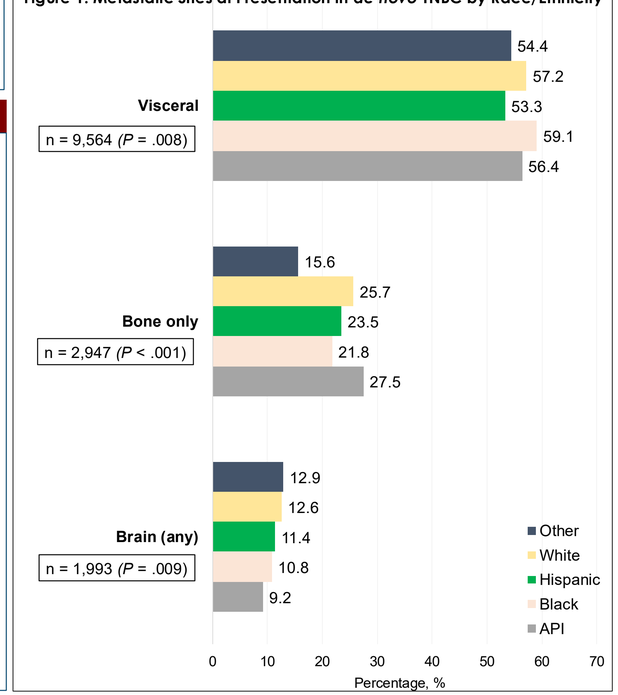


Table 2. Factors Associated with Treatment Initiation for *de novo* Metastatic TNBC

	No. of days between diagnosis and IO start	No. of days between diagnosis and chemo start	No. of days between diagnosis and RT start
	β (95% CI)	β (95% CI)	β (95% CI)
Age at diagnosis (per 10-year)	0.1 (-4.1, 4.2)	2.4 (1.3, 3.4)	-15.6 (-19.8, -11.5)
Race/ethnicity			
Black	7.1 (-2.1, 16.4)	3.0 (0.6, 5.3)	21.4 (11.9, 30.8)
API	-5.7 (-23.0, 11.7)	-0.8 (-6.6, 5.0)	31.9 (10.2, 53.6)
Hispanic	8.2 (-5.5, 21.8)	6.8 (2.6, 10.9)	34.9 (17.8, 52.0)
Other	23.1 (-17.8, 64.1)	9.9 (-0.6, 20.4)	6.8 (-34.6, 48.2)
White	0 [ref.]	0 [ref.]	0 [ref.]
Charlson-Deyo Comorbidity Index			
0	0 [ref.]	0 [ref.]	0 [ref.]
1	-3.6 (-13.9, 6.6)	0.3 (-2.4, 3.0)	-19.7 (-30.5, -9.0)
≥2	-2.3 (-17.5, 12.9)	-0.3 (-4.2, 3.7)	-33.0 (-47.8, -18.3)
Primary payer at diagnosis			
Private	0 [ref.]	0 [ref.]	0 [ref.]
Uninsured	0.9 (-17.4, 19.1)	2.8 (-1.7, 7.3)	-25.9 (-43.3, -8.5)
Medicaid	12.9 (2.0, 23.7)	2.4 (-0.5, 5.3)	-11.7 (-23.0, -0.3)
Medicare	9.6 (-0.8, 19.9)	3.0 (0.3, 5.7)	-7.7 (-18.5, 3.2)
Other	-18.7 (-61.9, 24.6)	4.3 (-4.8, 13.4)	-8.1 (-45.2, 28.9)
Percent no high school degree quartiles [b]			
≥ 15.3	0 [ref.]	0 [ref.]	0 [ref.]
9.1-15.2	-10.6 (-20.8, -0.4)	-1.7 (-4.4, 1.0)	-1.1 (-11.7, 9.6)
5.0-9.0	-17.1 (-28.8, -5.5)	-0.5 (-3.7, 2.6)	2.2 (-10.0, 14.5)
< 5.0	-22.2 (-35.7, -8.7)	-1.8 (-5.6, 2.0)	0.1 (-14.4, 14.6)
Median income quartiles [c]			
< $46,277	0 [ref.]	2.1 (-1.3, 5.5)	3.7 (-9.6, 16.9)
$46,227-$57,856	1.9 (-9.6, 13.3)	3.1 (0.2, 6.1)	-7.4 (-18.8, 4.0)
$57,857-$74,062	4.6 (-7.7, 16.8)	0.3 (-2.5, 3.1)	3.0 (-7.8, 13.8)
≥ $74,063	10.0 (-2.7, 22.7)	0 [ref.]	0 [ref.]
Facility type			
Academic/research	0 [ref.]	0 [ref.]	0 [ref.]
Community	8.2 (-6.8, 23.2)	-5.5 (-9.3, -1.6)	5.1 (-9.9, 19.9)
Comprehensive community	-3.7 (-11.8, 4.5)	-7.1 (-9.3, -4.9)	6.7 (-2.0, 15.4)
Integrated network	-5.8 (-15.5, 3.9)	-5.1 (-7.8, -2.4)	1.5 (-9.0, 12.0)

Key Takeaways

- Brain, bone-only, and visceral metastases at presentation varied by race/ethnicity.
- Racial and ethnic minority patients experienced **longer** time to initiate chemo or RT than White patients.
- IO initiation was **similar** across racial and ethnic groups when further adjusting for SES indicators.

Discussion and Conclusion

TNBC displayed heterogeneous patterns, with API patients having highest rates of bone-only metastatic disease and Black patients presenting more frequently with visceral metastasis at diagnosis.

IO initiation was delayed by 7.8 days for Black patients and 16.6 days for Hispanic patients compared to White patients; however, this differences were no longer significant after controlling for SES factors. This suggests that the clinical impetus for urgent treatment initiation based on metastatic site potentially mitigate some systemic challenges that contribute to delays for minority patients. TNBC's aggressive biology and poor prognosis may create a less tolerant environment to treatment delays regardless of race/ethnicity.

Limitations:

- NCDB does not collect incident metastatic cases, precluding us from deciphering differences in metastasis development.
- There remain other unmeasured characteristics, e.g., genetics, and genomics, that could better explain the observed disparities.
- NCDB also does not capture reasons for treatment delays, preventing distinction between patient-level, provider-level, and other system-level factors.
- Additionally, it lacks information regarding the specific treatment administered, which could lead to disparities in outcome.

In conclusion, this retrospective study found notable racial/ethnic and socioeconomic disparities in sites of metastases at presentation and treatment initiation for *de novo* metastatic TNBC in the U.S. More work is needed to alleviate these disparities and to improve care equity and treatment outcomes for all patients with metastatic TNBC.

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