Contribution of Sociodemographic Characteristics to Treatment Delays in Patients with *de novo* Metastatic HER2-Positive Breast Cancer

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Background

Outcomes for patients with *de novo* metastatic human epidermal growth factor receptor 2-positive (HER2+) breast cancer have dramatically improved due to advances in HER2-directed therapy.

Black and Hispanic patients persistently present with more advanced stage disease and experience worse survival outcomes compared to White patients.

Comprehensive analyses of the racial/ethnic and socioeconomic disparities in metastasis at presentation, treatment receipt, and initiation at the national level in the U.S. remain limited.

Methods & Materials

We analyzed a retrospective cohort of patients diagnosed with *de novo* metastatic HER2+ breast cancer between 2010 and 2022 using the National Cancer Database (NCDB).

Three metastatic sites at initial presentation were evaluated: brain, bone-only, and visceral (liver and/or lung).

We assessed three treatment modalities including chemotherapy (CT), HER2-directed therapy (TT), and radiotherapy (RT).

- Per the 2022 NCDB dictionary, targeted therapy drugs, including trastuzumab (Herceptin) and Pertuzumab (Perjeta), were classified as immunotherapy for breast cancer cases diagnosed in/after 2013.
- We categorized systemic therapy as CT alone or CT plus TT.

Time to treatment initiation was defined as the number of days between initial diagnosis and the start of treatment. This was compared across all treatment modalities and racial/ethnic groups.

Multivariable linear regression was performed to examine sociodemographic differences in time to initiation of systemic and localized (i.e., RT) therapies, respectively. Regression coefficients (β) and 95% CIs were calculated.

Results

A total of 27,972 patients with *de novo* metastatic HER2+ breast cancer were included. Mean age was 58.8 (SD 14.2) years; 69.0% were White, 17.5% Black, 7.8% Hispanic, and 4.6% Asian or Pacific Islander (API) per self-report.

Overall, 9.5% had brain metastases, 39.4% had bone-only metastases, and 58.2% had visceral metastases at initial presentation.

At the time of diagnosis, Black and Hispanic patients were younger, more often uninsured or Medicaid-insured, and more likely to reside in lower-education or lower-income areas (*P*<.001).

Table 1. Distributions of Time to Treatment Initiation for *de novo* Metastatic HER2+ Breast Cancer by Race/Ethnicity

	White	Black	API	Hispanic	Other	*P*
No. of days between diagnosis and start of CT						
Mean (SD)	41.9 (51.5)	49.9 (63.7)	38.2 (31.3)	57.1 (84.5)	61.7 (108.2)	<.001
Median (IQR)	31.0 (18.0, 49.0)	36.0 (21.0, 56.0)	29.5 (17.0, 49.5)	39.0 (23.0, 62.0)	28.0 (19.0, 62.0)	<.001
No. of days between diagnosis and start of TT						
Mean (SD)	47.2 (54.6)	54.6 (59.3)	46.2 (46.3)	57.2 (66.2)	40.5 (26.7)	<.001
Median (IQR)	35.0 (24.0, 55.0)	40.0 (27.0, 63.0)	35.0 (23.0, 54.0)	43.0 (28.0, 66.0)	34.0 (22.0, 52.0)	<.001
No. of days between diagnosis and start of RT						
Mean (SD)	125.2 (131.9)	133.7 (143.8)	153.1 (153.7)	152.6 (140.1)	117.1 (122.2)	<.001
Median (IQR)	61.0 (21.0, 222.0)	60.0 (22.0, 238.0)	131.0 (31.0, 240.0)	99.0 (32.0, 251.0)	60.0 (16.0, 219.5)	<.001

Figure 1. *De Novo* Metastatic Sites in HER2+ Breast Cancer across Racial/Ethnic Groups

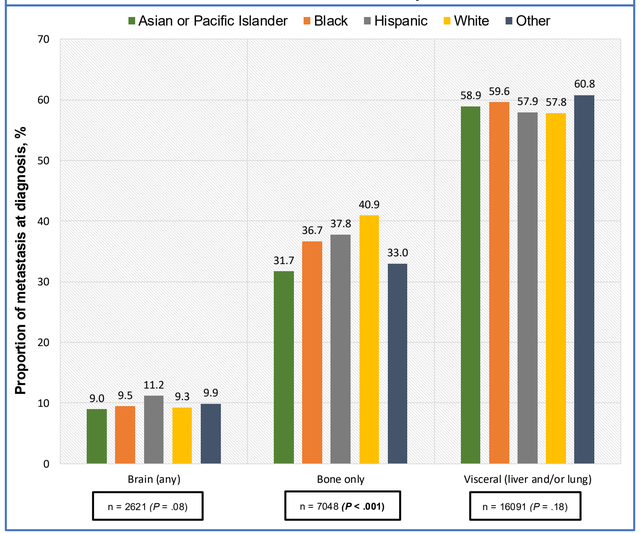


Table 2. Treatment Initiation Factors for de novo Metastatic HER2+ Breast Cancer

	No. of days between diagnosis & CT start	No. of days between diagnosis & TT start	No. of days between diagnosis & RT start
	β (95% CI)	**β (95% CI)**	**β (95% CI)**
Age at diagnosis (per 10-year)	0.54 (-1.56, 2.64)	1.00 (-0.23, 2.24)	**-18.86 (-22.96, -14.77)**
Race/ethnicity			
Black	**5.08 (0.10, 10.06)**	**5.71 (2.78, 8.63)**	8.03 (-1.72, 17.78)
API	-7.25 (-16.70, 2.20)	-1.98 (-6.70, 2.73)	**21.03 (4.86, 37.20)**
Hispanic	**15.57 (8.14, 23.00)**	**7.32 (3.22, 11.42)**	**23.00 (9.01, 36.98)**
Other	**22.04 (4.51, 39.58)**	-5.85 (-16.21, 4.52)	0.91 (-36.97, 38.79)
White	0 [reference]	0 [reference]	0 [reference]
Primary payer at diagnosis			
Uninsured	3.32 (-4.21, 10.84)	**5.77 (0.54, 11.00)**	**-25.25 (-41.35, -9.15)**
Private	0 [reference]	0 [reference]	0 [reference]
Medicaid	**8.05 (2.60, 13.50)**	**4.53 (1.40, 7.67)**	**-29.52 (-39.74, -19.29)**
Medicare	**5.46 (0.35, 10.57)**	**4.56 (1.40, 7.63)**	-1.87 (-11.92, 8.18)
Other	-2.16 (-21.23, 16.91)	-1.21 (-11.85, 9.44)	7.55 (-26.00, 41.10)
Percent no high school degree quartiles [b]			
≥ 15.3	**12.84 (5.87, 19.81)**	**8.46 (4.46, 12.46)**	8.40 (-4.72, 21.52)
9.1-15.2	**12.00 (5.99, 18.00)**	**8.20 (4.79, 11.61)**	-3.80 (-15.08, 7.47)
5.0-9.0	**7.57 (2.15, 12.99)**	1.64 (-1.46, 4.74)	-7.63 (-17.95, 2.68)
< 5.0	0 [reference]	0 [reference]	0 [reference]
Median income quartiles [c]			
< $46,277	0 [reference]	0 [reference]	0 [reference]
$46,227-$57,856	4.64 (-1.22, 10.51)	-1.16 (-4.60, 2.28)	3.21 (-8.09, 14.51)
$57,857-$74,062	1.34 (-4.62, 7.31)	-2.13 (-5.71, 1.46)	10.04 (-1.56, 21.64)
≥ $74,063	6.40 (-0.07, 12.86)	-0.70 (-4.48, 3.09)	8.07 (-4.13, 20.27)
Facility type			
Community	**-9.72 (-16.50, -2.94)**	-2.05 (-6.19, 2.09)	-11.98 (-25.71, 1.75)
Comprehensive community	-3.52 (-7.70, 0.66)	**-3.83 (-6.23, -1.44)**	-0.68 (-8.67, 7.31)
Academic/research	0 [reference]	0 [reference]	0 [reference]
Integrated network	**-7.19 (-12.21, -2.17)**	-2.87 (-5.82, 0.08)	-2.80 (-12.54, 6.94)

Key Points

- Bone-only metastasis is more common in White patients with *de novo* HER2+ breast cancer at presentation.
- Racial/ethnic minority patients experience significant delays in time to treatment initiation compared to White patients across all treatment modalities.
- Lower education areas and public / lack of insurance consistently delayed time to TT and CT initiation.
- Efforts should focus on enhancing health literacy, expanding insurance coverage, and improving care coordination infrastructure in disadvantaged communities.

Discussion & Conclusion

Bone-only metastatic disease, which is typically associated with a more favorable prognosis[1,2], was more common among White patients with HER2+ breast cancer, a trend that has not been previously described in the literature to our knowledge.

Black and Hispanic patients experienced longer delays (5.1-15.6 days) in TT and CT initiation, and Hispanic and API patients experienced significant delays in RT initiation (21-23 days). While recent evidence suggests narrowing racial gaps in TT receipt by 2018-2019[3,4], our findings demonstrate pervasive disparities using 2010 to 2022 data.

Regarding drivers of delay, lower education areas and insurance status (public or lack of insurance) consistently emerged as critical determinants of delayed time to treatment initiation for TT and CT but did not affect RT initiation.

In conclusion, substantial racial/ethnic disparities exist in metastatic patterns at presentation and timely treatment initiation, which persisted independent of clinical and system-level factors in this U.S. national sample of *de novo* HER2+ breast cancer patients.

Limitations:

- NCDB does not collect incident and recurrent metastatic cases, precluding us from deciphering differences in metastasis development and recurrence.
- There remain other unmeasured characteristics, e.g., marital status, genetics, and genomics, that may 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.

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Acknowledgements:
This work was supported in part by Breast Cancer Research Foundation (BCRF-23-071), NCI (P20 CA233307), and NIA (T32 AG000243). The contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCI and NIA.

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