Epidemiology of Human Epidermal Growth Factor Receptor 2-Positive Metastatic Breast Cancer in the United States in 2019

Naomi R.M. Schwartz[1], Sonia Pulgar[2], Susan Dennett[3]

[1]University of Washington, Seattle, WA; [2]Seattle Genetics, Bothell, WA; [3]Strategic Health Outcomes Inc, Indianapolis, IN

Background

- In the United States (US), breast cancer (BC) is the most common cancer among women; approximately 12.8% of women will develop BC in their lifetime.[1]
  - Approximately 5.6% of incident BC cases in the US are metastatic BC (MBC),[2] which has a 5-year survival rate of only 27.4% (compared with 89.9% for BC overall),[1] and limited treatment options.
- The human epidermal growth factor receptor 2-positive (HER2+) molecular subtype represents 20-30% of BC cases. HER2+ BC is biologically aggressive; it is likely to progress, particularly to distant metastases and is associated with poor overall survival.[1,3-5]
- Most population-based cancer registries in the US capture incident *de novo* MBC cases but not new cases of MBC resulting from progression of early breast cancer (EBC). Thus, registry data tend to underestimate the actual incidence of MBC.
  - This gap in knowledge poses challenges for researchers and policy makers, who rely on these data for healthcare and resource decision-making.

Objective

- To estimate the incidence of HER2+ MBC in the US in 2019, accounting for both *de novo* cases of HER2+ MBC and HER2+ EBC patients who progress to MBC.

Methods

- A patient flow model for 2019 was developed using data from the Surveillance, Epidemiology, and End Results (SEER) Program and a targeted literature review (**Figure 1**).
  - Estimates of BC incidence, proportions of incident BC cases that are metastatic and/or HER2+, and progression rates from EBC to MBC were extracted from studies published since 2010 that met quality criteria and were generalizable to the US population.
  - Studies were assessed for quality based on population inclusion/exclusion criteria, sample size, data source, time period, and methodology.
- A primary ("bespoke") analysis of SEER using SEER*Stat[6] was undertaken to estimate new cases of HER2+ MBC by calculating trends in incidence from 2010 to 2015 and applying those trends to subsequent years.
- A sensitivity analysis was conducted to evaluate the uncertainty and influence of each parameter on the overall estimate.

Results

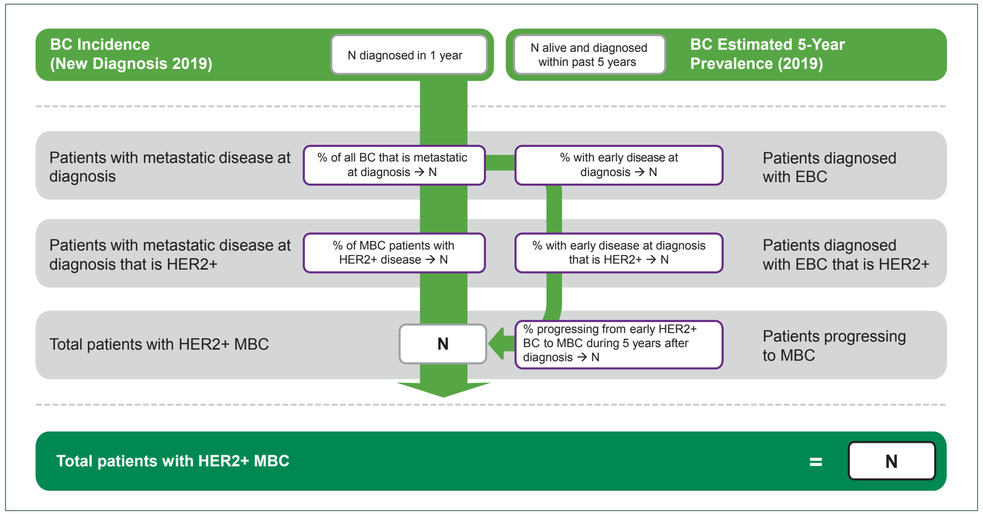
- 10 relevant sources[1,2,7-14] were identified from the targeted literature review. Of these, the 4 most robust sources[1,2,7,8] that provided data for at least 1 of the variables in the patient flow model were selected.
- Data from the selected publications were integrated into the model (**Figure 2**).
- The model estimates that 8,890 individuals were newly diagnosed with metastatic disease (n=3,946) or progressed to HER2+ MBC (n=4,944) in 2019 in the US.
  - Of 268,600 patients with incident BC in 2019 (SEER), an estimated 15,042 (5.6%) had MBC at diagnosis, of whom 3,946 (26.2%) were HER2+.
  - Among patients with EBC at diagnosis (n=253,558), it is estimated that 38,034 (15.0%) were HER2+, and that 4,944 patients progressed to HER2+ MBC during 2019.
- In sensitivity analyses, the estimated annual incidence ranged from 6,044 to 9,474 cases of HER2+ MBC (**Table 1**). Using trends from SEER data, the estimated number of new HER2+ MBC cases in 2019 was 8,380.
  - The most influential parameters were BC incidence and the proportion of incident MBC that is HER2+ (**Figure 3**).

Table 1. Estimated number of new patients diagnosed with or progressing to HER2+ MBC in the United States, 2019: primary and sensitivity analyses

Stage	Lowest	Highest	Median	Mean	Best published[a]	Bespoke SEER trended
BC incidence[1,9]	234,087 (GLOBOCAN 2018)	268,600 (SEER 2019)	251,344	251,344	268,600 (SEER 2019)	268,600 (SEER 2019)
Incident MBC[2,6,7,10-12,b]	4.7% (Press 2017)	5.8% (Xiong 2018)	4.9%	5.2%	5.6% (SEER* Explorer)	3.9% (SEER*Stat extrapolated)
Incident EBC (calculated)[c]	95.3%	94.2%	95.1%	94.8%	94.0%	96.2%
Incident MBC that is HER2+[7,10,11,13,14]	20.5% (Martin 2017)	27.6% (Press 2017)	21.7%	23.4%	26.2% (Gong 2017)	28.4% (SEER*Stat extrapolated)
Incident EBC that is HER2+[7,10-13]	13.0% (Martin 2017)	15.7% (Press 2017)	13.3%	14.0%	15.0% (Gong 2017)	16.2% (SEER*Stat extrapolated)
Incident HER2+ EBC that progresses within 5 years[8,d]	13.0% (Malmgren 2019)	13.0% (Malmgren 2019)	13.0%	13.0%	13.0% (Malmgren 2019)	13.0% (Malmgren 2019)
HER2+ MBC (calculated from incidence)	**6,044**	**9,474**	**6,805**	**7,378**	**8,890**	**8,380**

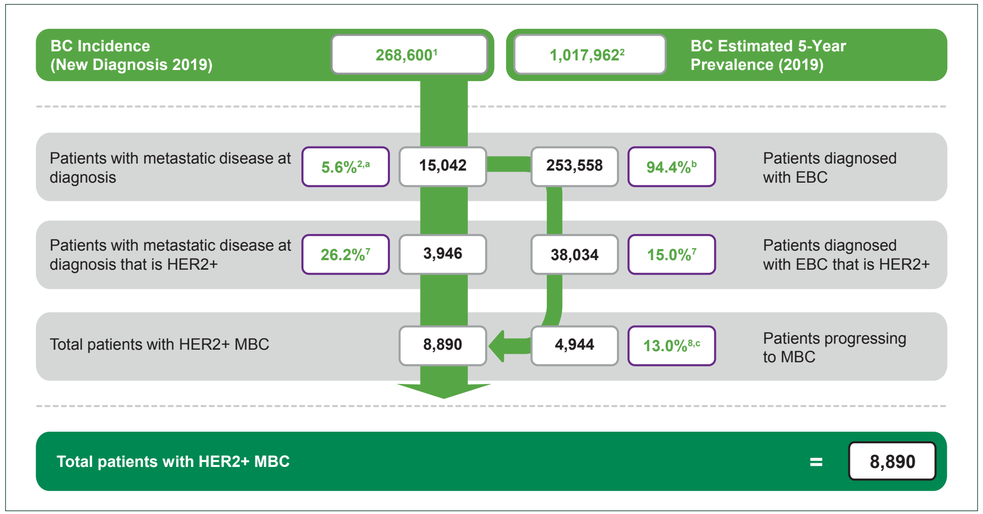
[a]Best estimate from the literature based on assessment of population inclusion/exclusion criteria, sample size/data source, time period of data source, and study quality and methodology.
[b]Metastatic or distant disease only; does not include regional disease per SEER classification.
[c]Calculated as 1-(proportion metastatic at diagnosis).
[d]Estimated rate of progression of 13.0% is assumed to apply over a 5-year period at a rate of 2.6% progressing each year.
BC, breast cancer; EBC, early breast cancer; HER2+, human epidermal growth factor receptor 2-positive; MBC, metastatic breast cancer; SEER, Surveillance, Epidemiology, and End Results.

Figure 1. Overview of patient flow model to estimate annual incidence of HER2+ MBC



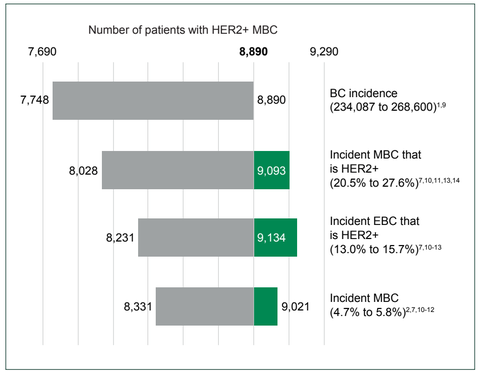
BC, breast cancer; EBC, early breast cancer; HER2+, human epidermal growth factor receptor 2-positive; MBC, metastatic breast cancer.

Figure 2. Estimated annual incidence of HER2+ MBC in the United States, 2019



[a]Metastatic or distant disease only; does not include regional disease per SEER classification.
[b]Calculated as 1-(proportion metastatic at diagnosis).
[c]Estimated rate of progression of 13.0% is assumed to apply over a 5-year period at a rate of 2.6% progressing each year.
BC, breast cancer; EBC, early breast cancer; HER2+, human epidermal growth factor receptor 2-positive; MBC, metastatic breast cancer; SEER, Surveillance, Epidemiology, and End Results.

Figure 3. Sensitivity analysis of the estimated incidence of HER2+ MBC in the United States, 2019



Estimates for individual variables were adjusted from low to high values, with all other variables set to the best estimate across identified references. Proportion of incident HER2+ EBC that progresses within 5 years is not included in the plot as only one relevant source was identified.[8]
BC, breast cancer; EBC, early breast cancer; HER2+, human epidermal growth factor receptor 2-positive; MBC, metastatic breast cancer.

Discussion

- This model provides a data-driven approach to estimate the annual incidence of HER2+ MBC in the US.
- Model inputs can be updated as new data become available, allowing estimation of incidence in future years.
- The accuracy of this model is dependent on the availability and validity of published data. Although sources were assessed for quality, data for some model inputs were scarce. Sensitivity analyses demonstrate the extent of uncertainty in the results.
- Despite some limitations, because the model incorporates incident HER2+ MBC that results from the progression of EBC, it provides a more accurate estimate of HER2+ MBC incidence than is currently available for the US.

References

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Program: cancer stat facts: female breast cancer; 2019 [URL: https://seer.cancer.gov/statfacts/html/breast.html]. Accessed February 28, 2020. **2.** National Cancer Institute. Surveillance, Epidemiology, and End Results Program: SEER*Explorer; 2019 [URL: https://seer.cancer.gov/explorer/]. Accessed February 28, 2020. **3.** Ignatov A, et al. J Cancer Res Clin Oncol. 2018;144(7):1347-55. **4.** van Maaren MC, et al. Int J Cancer. 2019;144(2):263-72. **5.** Gabos Z, et al. J Clin Oncol. 2006;24(36):5658-63. **6.** National Cancer Institute. Surveillance, Epidemiology, and End Results Program: SEER*Stat; 2019 [URL: https://seer.cancer.gov/seerstat/]. Accessed October 29, 2019. **7.** Gong Y, et al. Sci Rep. 2017;7:45411. **8.** Malmgren J, et al. Breast Cancer Res Treat. 2019;174(2):505-14. **9.** International Association of Cancer Registries. GLOBOCAN database; 2019 [URL: http://gco.iarc.fr/]. Accessed November 4, 2019. **10.** Xie J, et al. Cancer Epidemiol Biomarkers Prev. 2019;28(2):283-92. **11.** Press DJ, et al. Clin Exp Metastasis. 2017;34(8):457-65. **12.** Xiong Z, et al. Cancer Manag Res. 2018;10:287-95. **13.** Martin AM, et al. JAMA Oncol. 2017;3(8):1069-77. **14.** Dalvi T, et al. Cancer Res. 2019;79(4_suppl):Abstract P1-09-14.

ACKNOWLEDGMENTS: Medical writing support was provided by Ann Cameron of Curo, a division of Envision Pharma Group, and funded by Seattle Genetics.

Corresponding author: Naomi Schwartz (nschwartz@seagen.com).

Poster presented at the Academy of Managed Care Pharmacy (AMCP) 2020 Virtual Learning Event, April 20–24, 2020