Defining the prognosis of estrogen receptor low-positive de novo metastatic breast cancer (dnMBC)

Klugman, MF, MD, MS[1] ; Aboumrad, M, PhD[2]; Chen, R, PhD[1]; Marshall, CH, MD, MPH[1]; Canzoniero, JV, MD, MS[1]; Wolff, AC, MD[1]; and Visvanathan, K, MD, MHS[1,2]

[1]Department of Oncology, Sidney Kimmel Cancer Center, Johns Hopkins School of Medicine, Baltimore, MD; [2]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Background and Objectives

- There are limited studies evaluating risk groups and outcomes in ER low-positive metastatic breast cancer
- **Primary objective**: Compare the overall survival (OS) of patients with HER2- dnMBC by estrogen receptor (ER) status (negative, low-positive, high-positive)
- **Secondary objective**: Identify prognostic groups among patients with ER low-positive dnMBC
- **Exploratory objective**: Among the subset of patients with ER low-positive dnMBC, compare survival by initial treatment regimens

Methods and Materials

- **Design:** Retrospective cohort study using data from the National Cancer Database (NCDB)
- **Eligibility criteria:** Adults with HER2-negative dnMBC diagnosed between 2018-2021 (Figure 1)
- **Primary outcome:** OS
- **Exposures:** 1) ER status and 2) ER status
- with ER low-positive patients stratified by progesterone receptor (PR) status (<1% vs 1-100%)
- **Covariates:** Sociodemographics, clinical features, treatment receipt.
- First-course treatments in NCDB are defined as systemic therapy received before disease progression
- "Chemotherapy" in NCDB includes cytotoxic chemotherapy and CDK4/6 inhibitors (CDK4/6i).
- First-course treatment assumptions:
  - "Chemotherapy" without endocrine therapy = cytotoxic chemotherapy alone
  - "Chemotherapy" start prior to endocrine therapy = cytotoxic chemotherapy → maintenance endocrine therapy (±CDK4/6i)
  - "Chemotherapy" start date on or after endocrine therapy start date = endocrine therapy ±CDK4/6i
  - Endocrine therapy without "chemotherapy" = endocrine therapy alone
- **Analyses:** Age-adjusted and Multivariable Cox regressions. Interaction assessed via Wald test

Results

Figure 1. Cohort creation

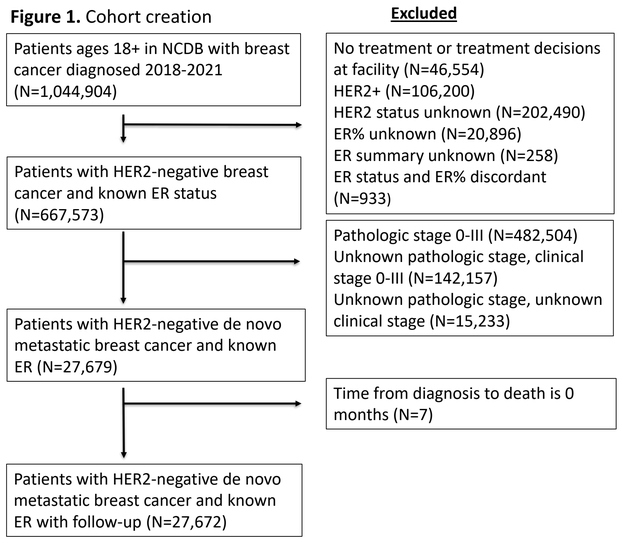
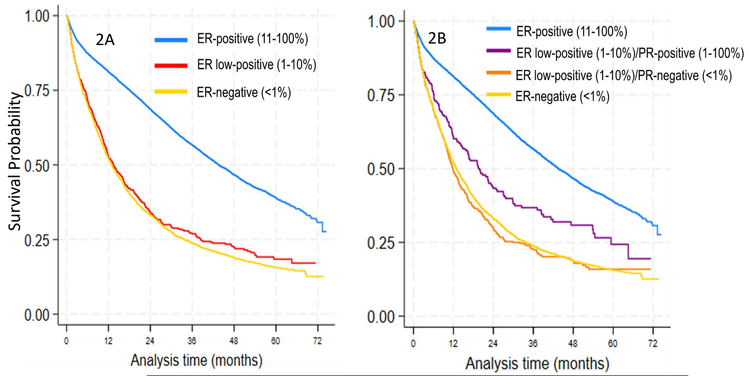


Table 1. Characteristics of patients with HER2-negative dnMBC, by ER status

Variable	ER-negative (<1%) N=5,760	ER low-positive (1-10%) N=699	ER-positive (11-100%) N=21,213
Age [Mean (SD)] years	62 (14)	62 (14)	64 (14)
Sites of metastatic disease			
Not bone-only	86%	81%	61%
Bone-only	14%	19%	39%
Unknown	<1%	<1%	<1%
Progesterone receptor status			
Negative (<1%)	93%	68%	17%
Positive (1-100%)	7%	32%	83%
Unknown	<1%	1%	<1%
Grade/Differentiation			
Low grade/well	1%	2%	10%
Intermediate grade/moderate	15%	20%	45%
High-grade/poorly/un-differentiated	65%	58%	24%
Unknown	19%	20%	21%

Figure 2. OS by ER status (2A) and ER-PR status (2B)



ER-PR status	Median survival (95%CI) (months)
ER-positive	43.6 (42.7-44.7)
ER low-positive/PR-positive	19.8 (14.8-24.8)
ER low-positive/PR-negative	11.8 (10.6-13.5)
ER-negative	12.9 (12.5-13.6)

Table 2. Multivariable Cox regression assessing OS by ER status and ER-PR status

ER status	N (%)	Adjusted HR (aHR) (95%CI)
ER-negative	5467 (21)	1 (ref)
ER low-positive	663 (3)	1.04 (0.94-1.14)
ER-positive	20177 (77)	**0.50 (0.48-0.52)**
ER-PR status	**N (%)**	**aHR (95%CI)**
ER-negative	5467 (21)	1 (ref)
ER low-positive/PR-negative	450 (2)	1.14 (1.02-1.27)
ER low-positive/PR-positive	209 (1)	**0.84 (0.71-1.00)**
ER-positive	20177 (77)	**0.50 (0.48-0.52)**

Both models are adjusted for age, sites of disease, treatment receipt, race, ethnicity, comorbidities, and insurance

Table 2. Adjusted overall survival by treatments among patients with ER low-positive dnMBC, overall and stratified by PR status [1]

	ER low-positive (1-10%) overall		ER low-positive/PR-negative (<1%)		ER low-positive/PR-positive (1-100%)	
First-course treatment	**N (%)**	**aHR (95%CI)[1] N=541**	**N (%)**	**aHR (95%CI)[1] N=368**	**N (%)**	**aHR (95%CI)[1] N=173**
Chemo-therapy alone	327 (60)	1 (ref)	258 (70)	1 (ref)	69 (40)	1 (ref)
Chemo-therapy → maintenance endocrine therapy (±CDK4/6i)	68 (13)	**0.62 (0.44-0.88)**	36 (10)	**0.52 (0.33-0.82)**	32 (19)	0.76 (0.43-1.35)
Endocrine therapy + CDK4/6i	68 (13)	0.70 (0.49-1.01)	40 (11)	0.70 (0.46-1.08)	28 (16)	0.75 (0.38-1.46)
Endocrine therapy alone	78 (14)	1.34 (0.96-1.89)	34 (9)	**2.20 (1.44-3.35)**	44 (25)	0.82 (0.46-1.46)

Adjusted for age, sites of disease, comorbidities, race/ethnicity, and insurance. The unstratified analysis is also adjusted for PR status

[1]Pinteraction=0.01

Conclusions

- PR-positivity identifies a subgroup of ER low-positive dnMBC patients with longer survival than ER-negative patients.
- Treatments incorporating endocrine therapy may be appropriate to consider as part of the initial treatment for patients with ER low-positive dnMBC.

- Strengths: real-world data from a large, nationwide cohort
- Limitations: lack of detailed treatments, no cause of death data, no central review of ER status, unmeasured confounders impacting treatment choice

Contact

Madelyn Klugman and Kala Visvanathan
Johns Hopkins Sidney Kimmel Comprehensive Cancer Center
mklugma2@jh.edu; kvisvan1@jhu.edu
@KlugmanMaddie

Acknowledgements

This research was supported by grants from the National Cancer Institute (P30CA006973) and the Breast Cancer Research Foundation.

Key References

1. Allison KH, Hammond MEH, Dowsett M, et al. Estrogen and Progesterone Receptor Testing in Breast Cancer: ASCO/CAP Guideline Update. *J Clin Oncol*. 2020;38(12):1346-1366. doi:10.1200/JCO.19.02309
2. National Comprehensive Cancer Network. Breast Cancer. Version 4.2025. NCCN. Accessed July 30, 2025. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
3. Choong GM, Hoskin TL, Boughey JC, Ingle JN, Goetz MP. Endocrine Therapy Omission in Estrogen Receptor–Low (1%-10%) Early-Stage Breast Cancer. J Clin Oncol. 2025;43(16):1875-1885. doi:10.1200/JCO-24-02263

This presentation is the intellectual property of the author/presenter. Contact them at mklugma2@jh.edu for permission to reprint and/or distribute.

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com