HR+/HER2- Metastatic Breast Cancer:
A Heterogenous Disease With Varied Clinical Outcomes

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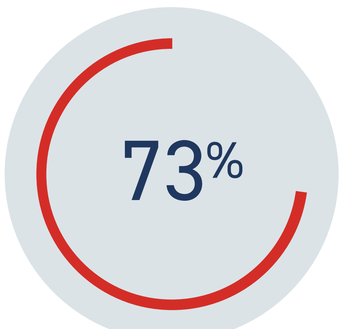
Hormone receptor–positive (HR+)/HER2-negative (HER2-) metastatic breast cancer (MBC) is a heterogenous disease with distinctive subtypes and associated prognoses



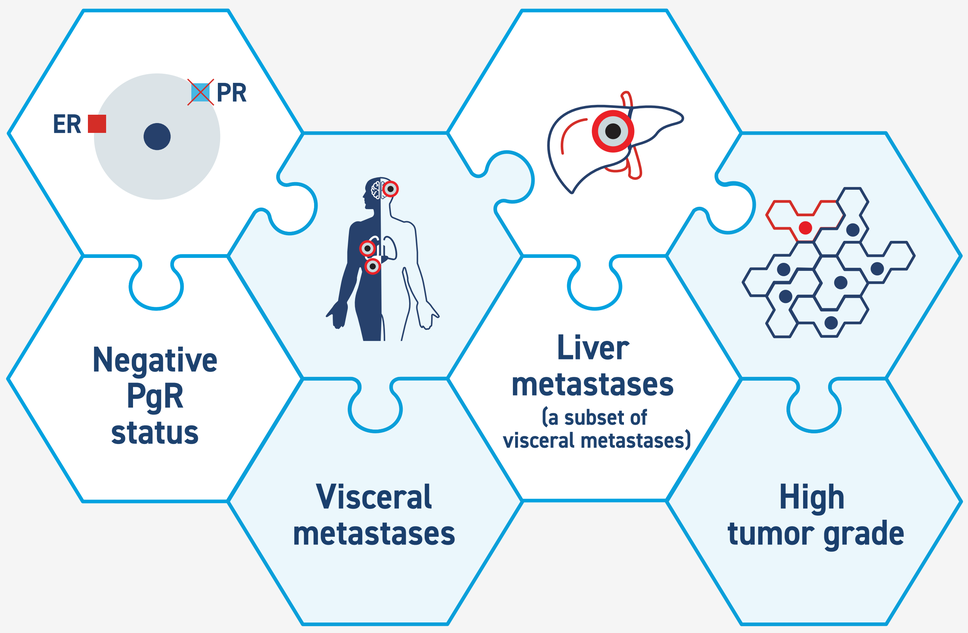
HR+/HER2- is the most common subtype of invasive breast cancer, representing **approximately 73%** of all cases[1]

HR+/HER2- breast cancer can be further categorized into different subtypes based on[2,3]:

- Gene expression patterns
- Clinical and biological properties
- Histology
- Response to treatment

Approximately 60% of patients with advanced HR+/HER2- breast cancer have ≥1 disease-related factor more likely to confer a poor prognosis[4]

Factors include[4]:

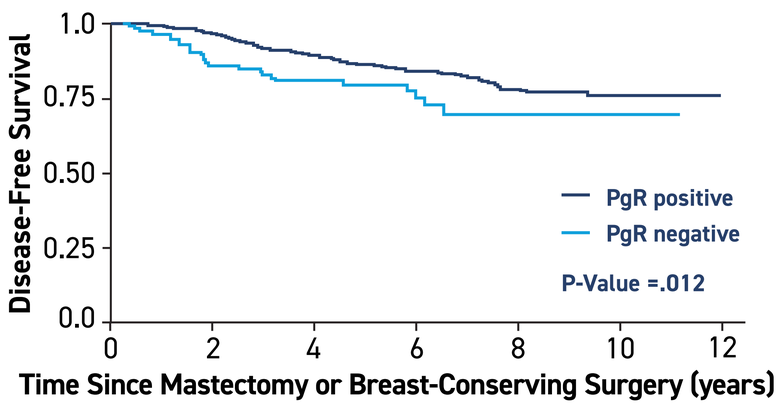


There is overlap in the presence of negative PgR status, visceral metastases, and high tumor grade, with 18% of patients harboring 2 disease-related factors and 3% of patients harboring all 3 factors[4]

Patients with HR+/HER2- MBC harboring ≥1 prognostic factor displayed a significantly shorter real-world progression-free survival and overall survival (OS) compared to those with no prognostic factors[5]

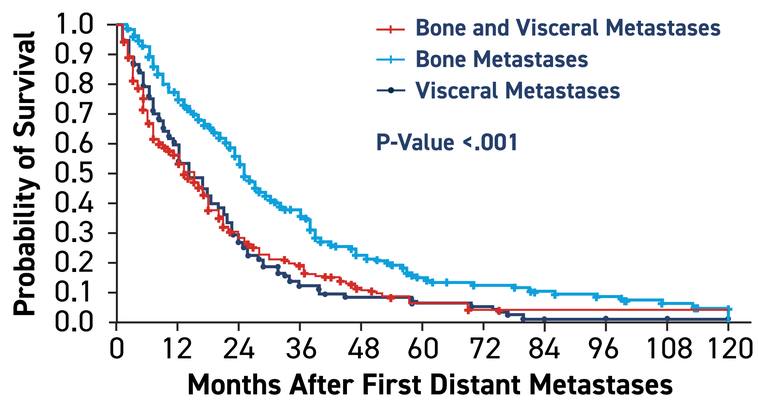
Outcomes for patients with HR+/HER2- MBC vary depending on the presence of certain prognostic factors[6-8]

PgR Status



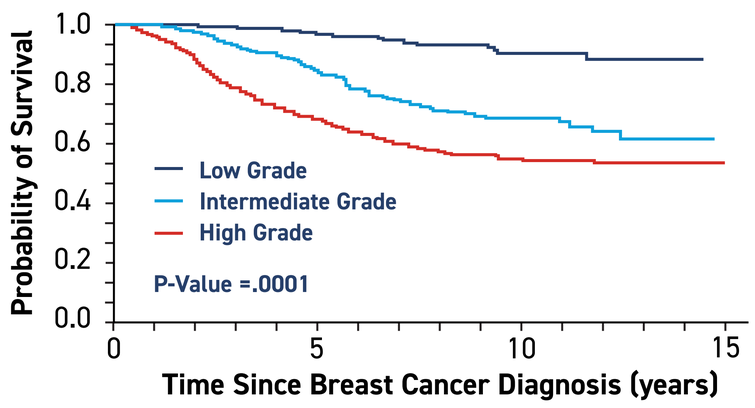
Patients who lack PgR expression displayed a lower disease-free survival than patients with PgR expression[6]

Site of Metastases



Patients who have visceral metastases had a worse OS than patients with bone-only metastases[7]

Tumor Grade



Patients with high-grade tumors or intermediate-grade tumors showed worse OS than patients with low-grade tumors[8]

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2. Eliyatkin N, et al. *J Breast Health*. 2015;11(2):59-66.
3. Prat A, et al. *Breast*. 2015;24(suppl 2) 2:S26-S35.
4. Davie A, et al. *ESMO Open*. 2021;6(4):100226.
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Standard treatment for patients with HR+/HER2- MBC includes cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) + endocrine therapy (ET)[1,2]

Treatment with CDK4/6i + ET improves outcomes for patients with HR+/HER2- MBC when compared to treatment with ET alone[3,4]

In a pooled analysis of randomized trials of ET ± CDK4/6i in patients with HR+/HER2- MBC approved by the US Food and Drug Administration, **the addition of CDK4/6i** resulted in[a,3]:

41% **reduction in the risk of disease progression or death**

Patients treated with CDK4/6i + ET in first-line (1L) or greater settings derived similar progression-free survival benefits, regardless of de novo metastatic status, site of metastasis, and histological classification, when compared to those treated with ET alone

[a]CDK4/6i in the pooled analysis included palbociclib, ribociclib, and abemaciclib; ET in the pooled analysis included aromatase inhibitor or fulvestrant.

Use of CDK4/6i in the real-world setting

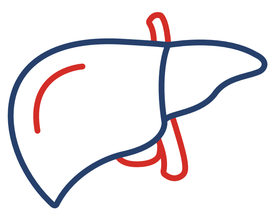
CDK4/6i are becoming more widely used in the 1L setting for patients with HR+/HER2- MBC; however, greater use of CDK4/6i would likely maximize patient outcomes[5,6]

In a study of 906 patients with HR+/HER2- advanced breast cancer treated in the 1L setting between October 2019 and February 2020[7]:

Did not receive CDK4/6i	Received any CDK4/6i regimens		
	57%		
43%	CDK4/6i + aromatase inhibitor	CDK4/6i + fulvestrant	Other CDK4/6i regimen
	74%	24%	2%

Prognostic factors lead to heterogeneity of treatment outcomes for patients with HR+/HER2- MBC[8]

Among 207 patients with HR+/HER2- MBC treated with CDK4/6i in the 1L real-world setting:



Presence of liver metastases resulted in a **2.0x higher risk of progression or death**, and **2.6x shorter OS** when compared to no liver metastases

Presence of metastases beyond the bone yielded **2.2x higher risk of progression or death**, and **1.3x shorter OS** compared to bone-only metastases

As healthcare providers, it is important to identify patients with HR+/HER2- MBC who may be at risk for less optimal outcomes based on clinical and pathological factors, and to understand the benefits of CDK4/6i + ET for 1L treatment

1. Gennari A, et al. *Ann Oncol*. 2021;32(12):1475-1495.
2. Burstein HJ, et al. *J Clin Oncol*. 2021;39(35):3959-3977.
3. Gao JJ, et al. *Lancet Oncol*. 2020;21(2):250-260.
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