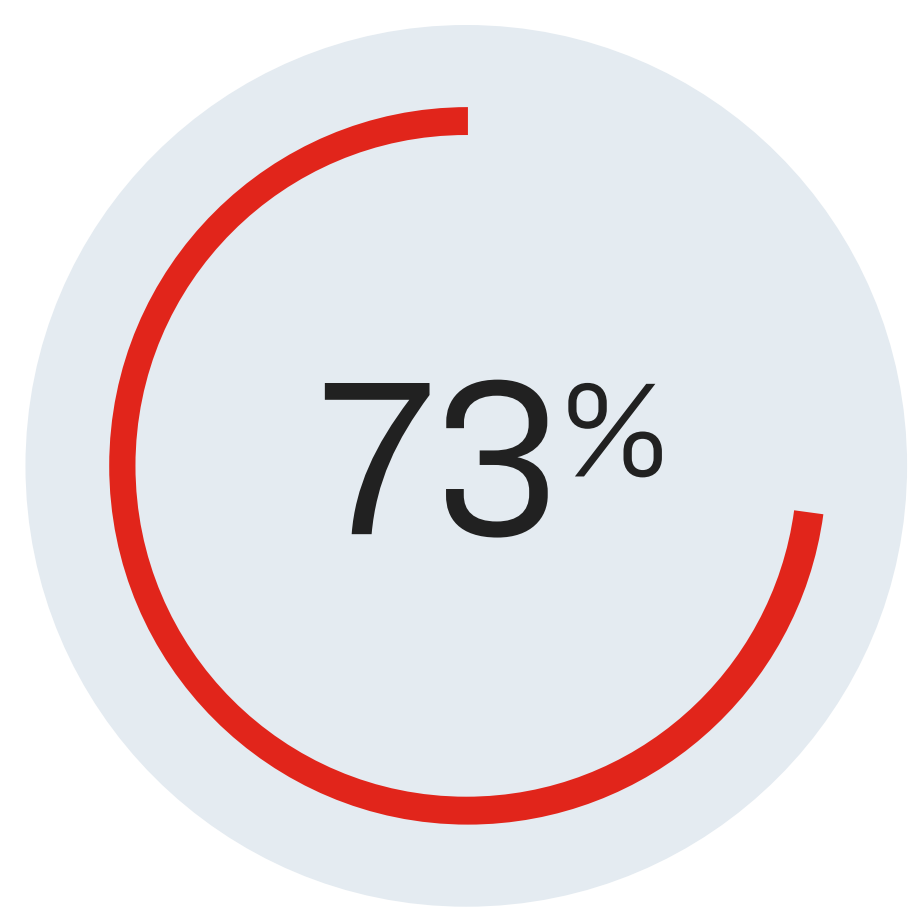


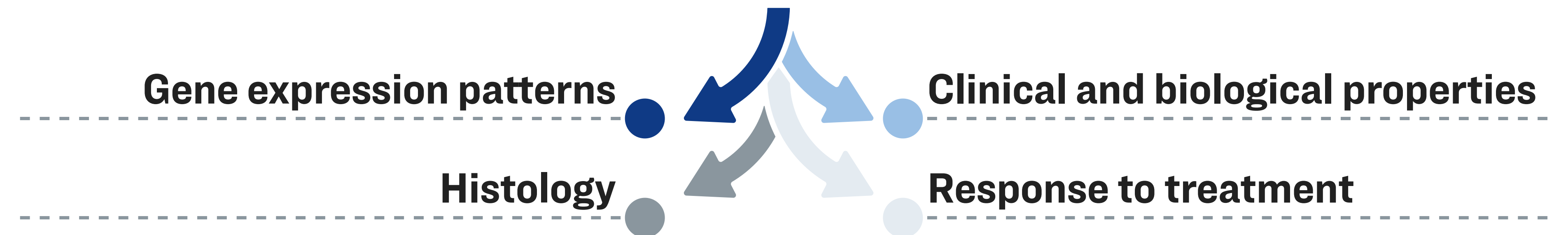
HR+/HER2- Metastatic Breast Cancer: A Heterogenous Disease With Varied Clinical Outcomes

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



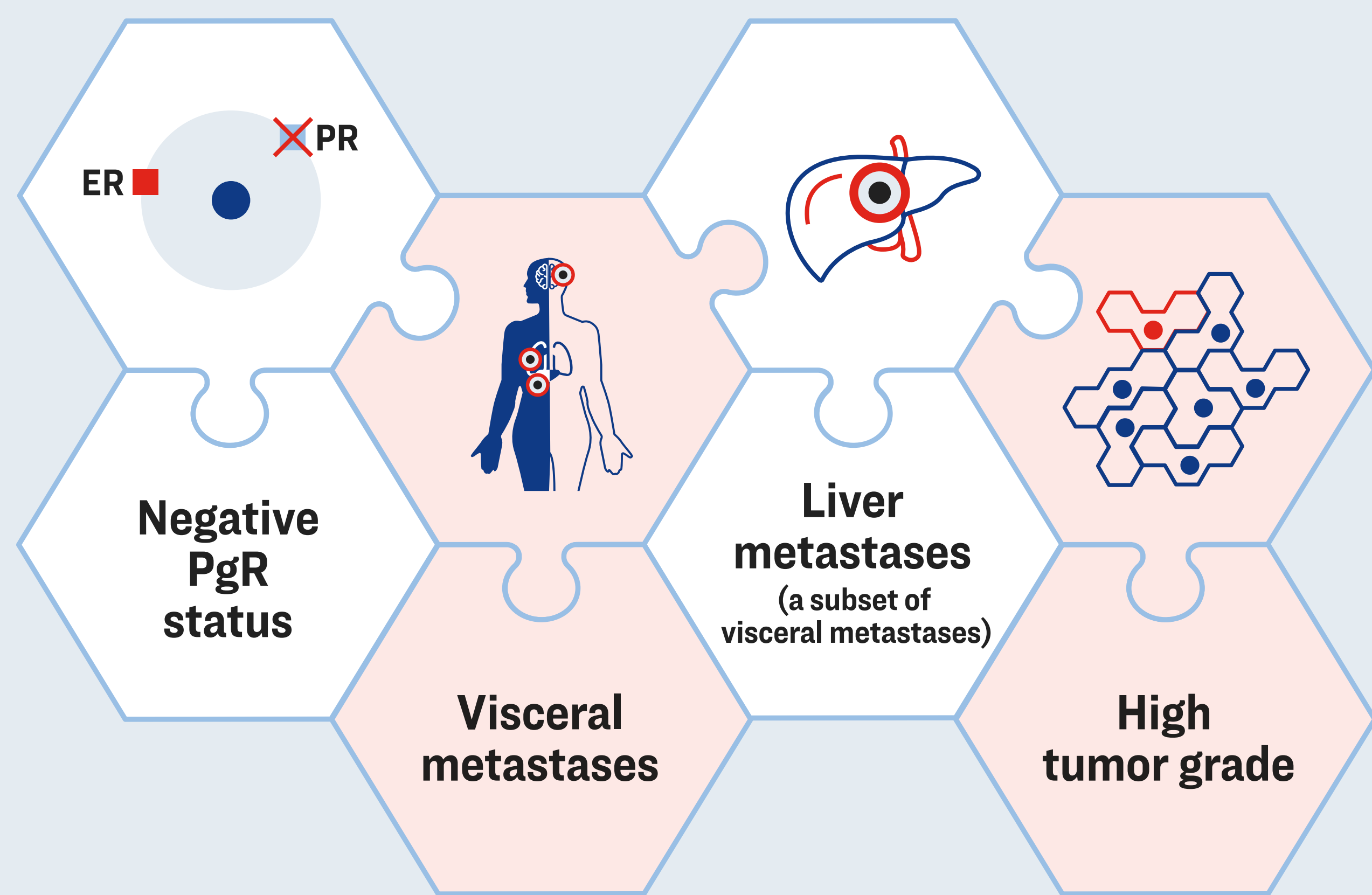
HR+/HER2- is the most common subtype of invasive breast cancer, representing **approximately 73%** of all cases¹

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



Approximately **60%** of patients with advanced HR+/HER2- breast cancer have ≥ 1 disease-related factor more likely to confer a poor prognosis⁴

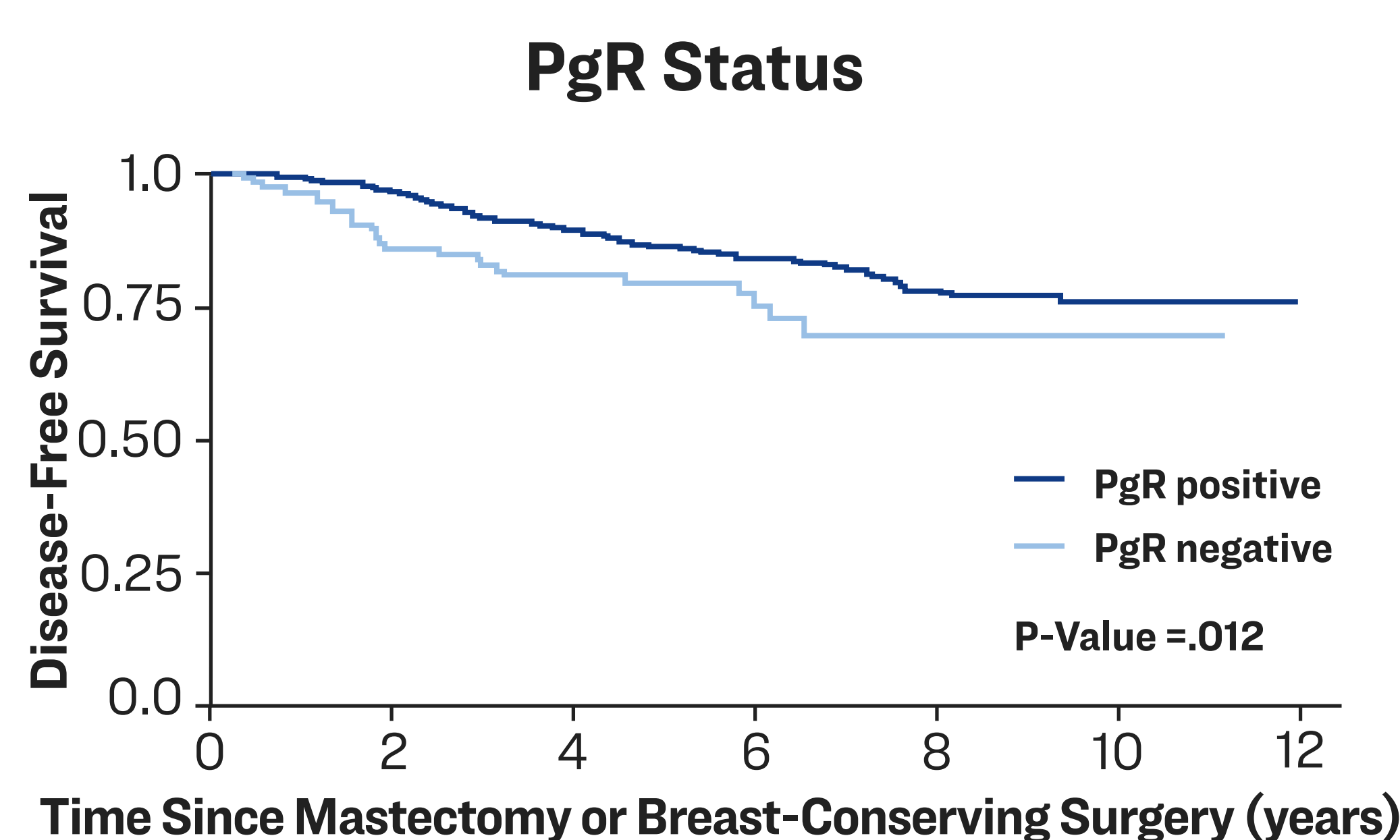
Factors include⁴:



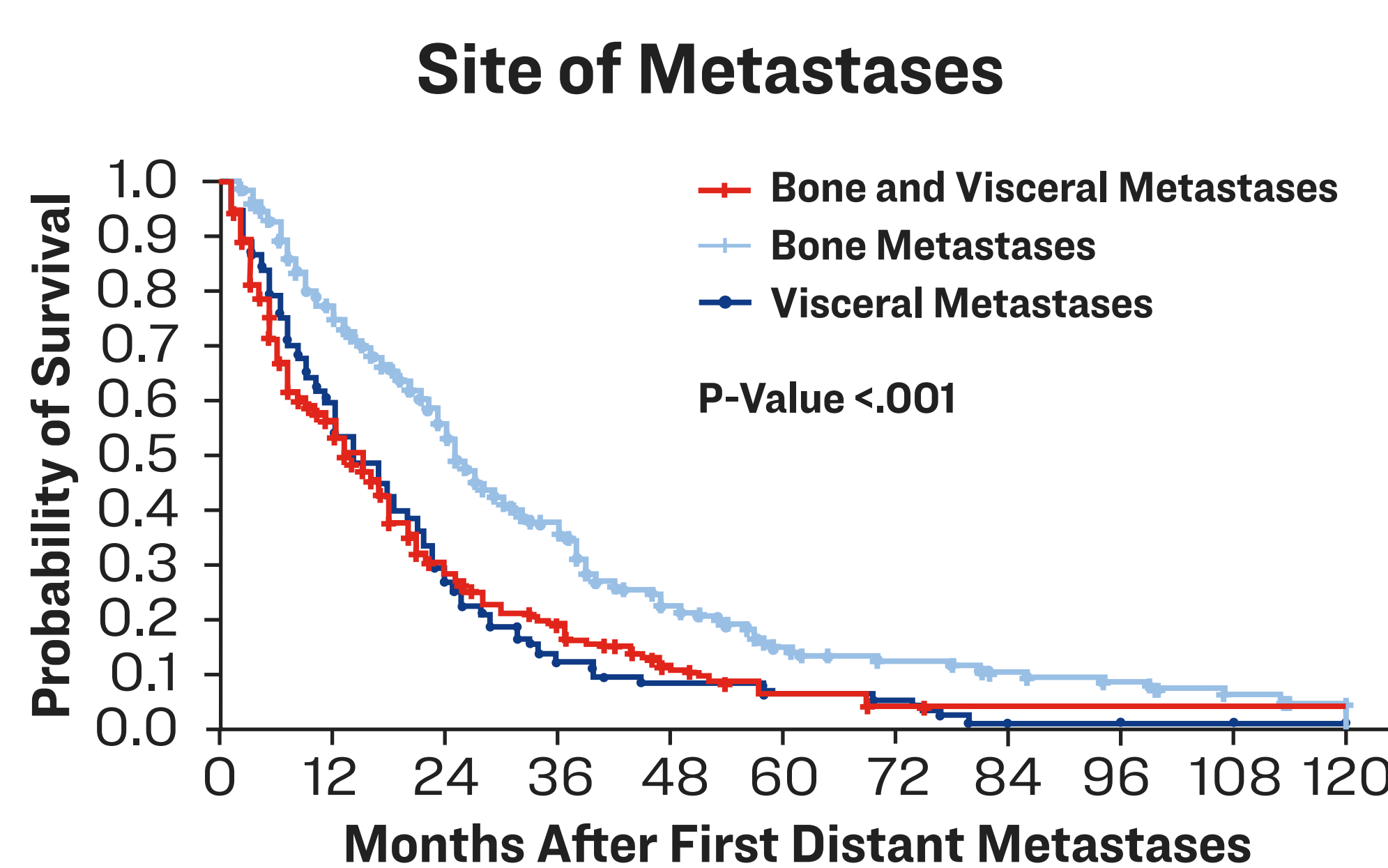
There is overlap in the presence of negative PgR status, visceral metastases, and high tumor grade, with 18% of patients harboring 2 disease-related factors and 3% of patients harboring all 3 factors⁴

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 factors⁵

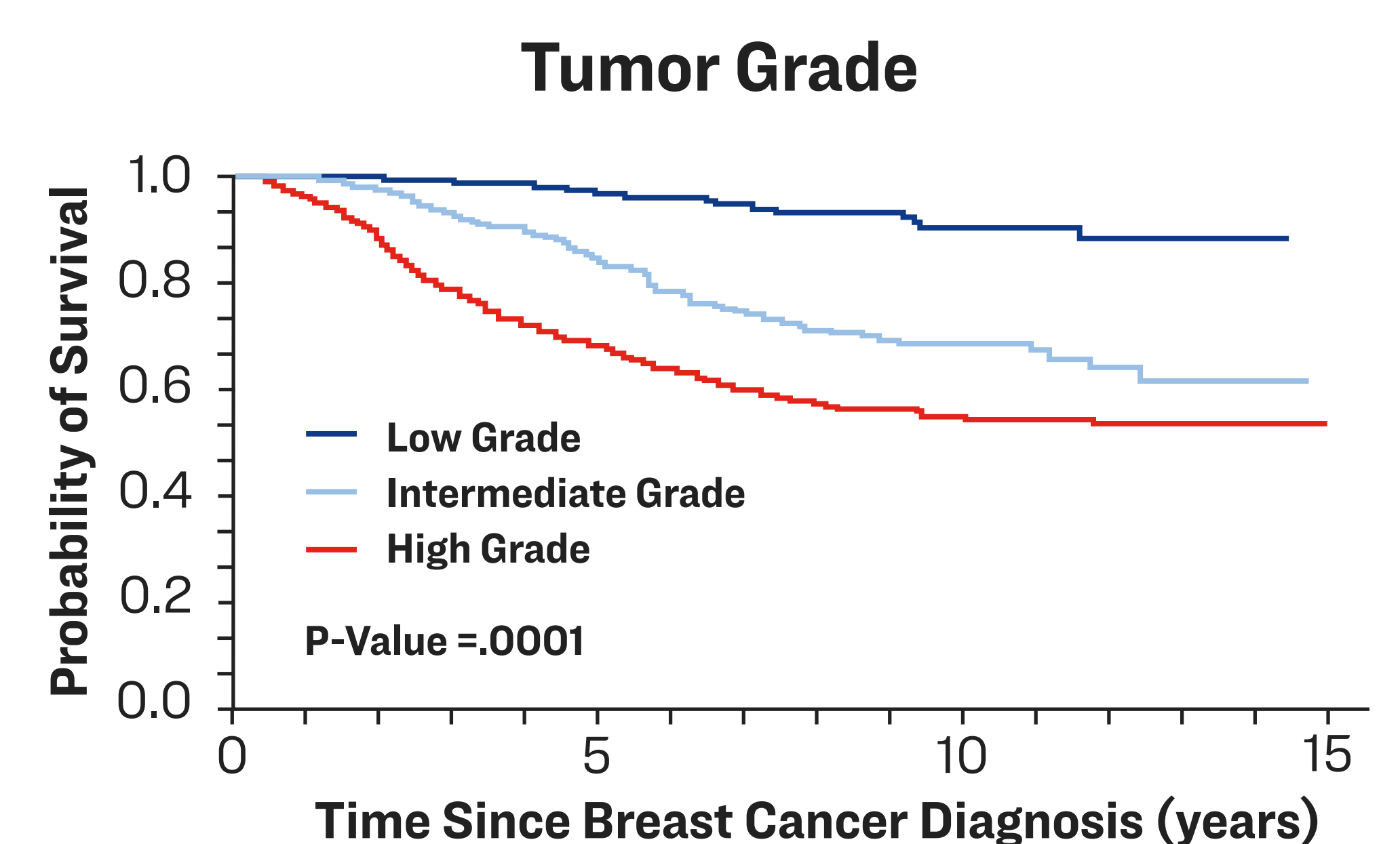
Outcomes for patients with HR+/HER2- MBC vary depending on the presence of certain prognostic factors⁶⁻⁸



Patients who lack PgR expression displayed a lower disease-free survival than patients with PgR expression⁶



Patients who have visceral metastases had a worse OS than patients with bone-only metastases⁷



Patients with high-grade tumors or intermediate-grade tumors showed worse OS than patients with low-grade tumors⁸

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

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}

41% reduction in the risk of disease progression or death

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}:

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

^aCDK4/6i 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 2020⁷:

Did not receive CDK4/6i

Received any CDK4/6i regimens

43%

57%

CDK4/6i +
aromatase
inhibitor

CDK4/6i +
fulvestrant

Other
CDK4/6i
regimen

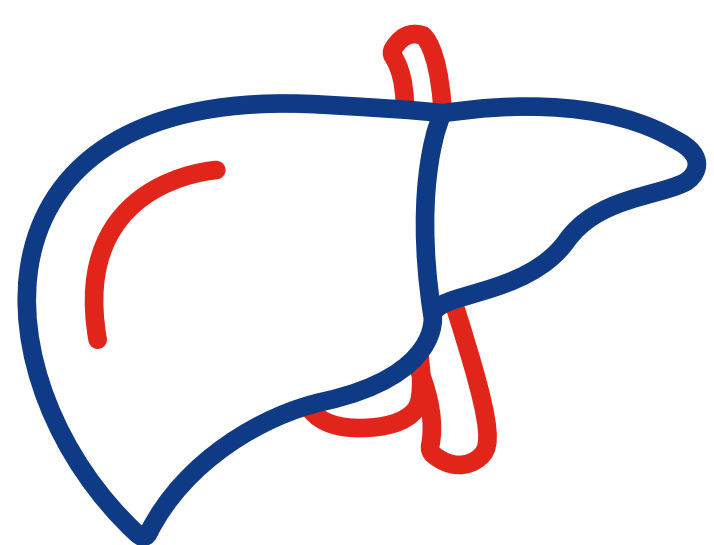
74%

24%

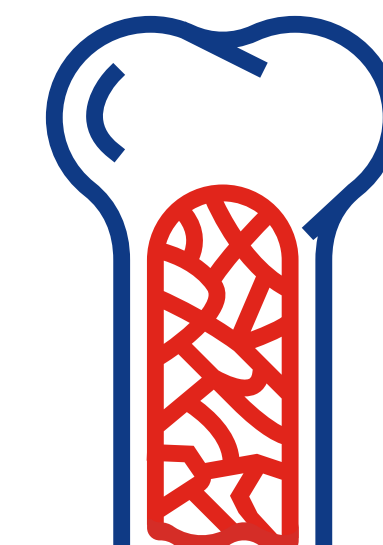
2%

Prognostic factors lead to heterogeneity of treatment outcomes for patients with HR+/HER2- MBC⁸

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



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