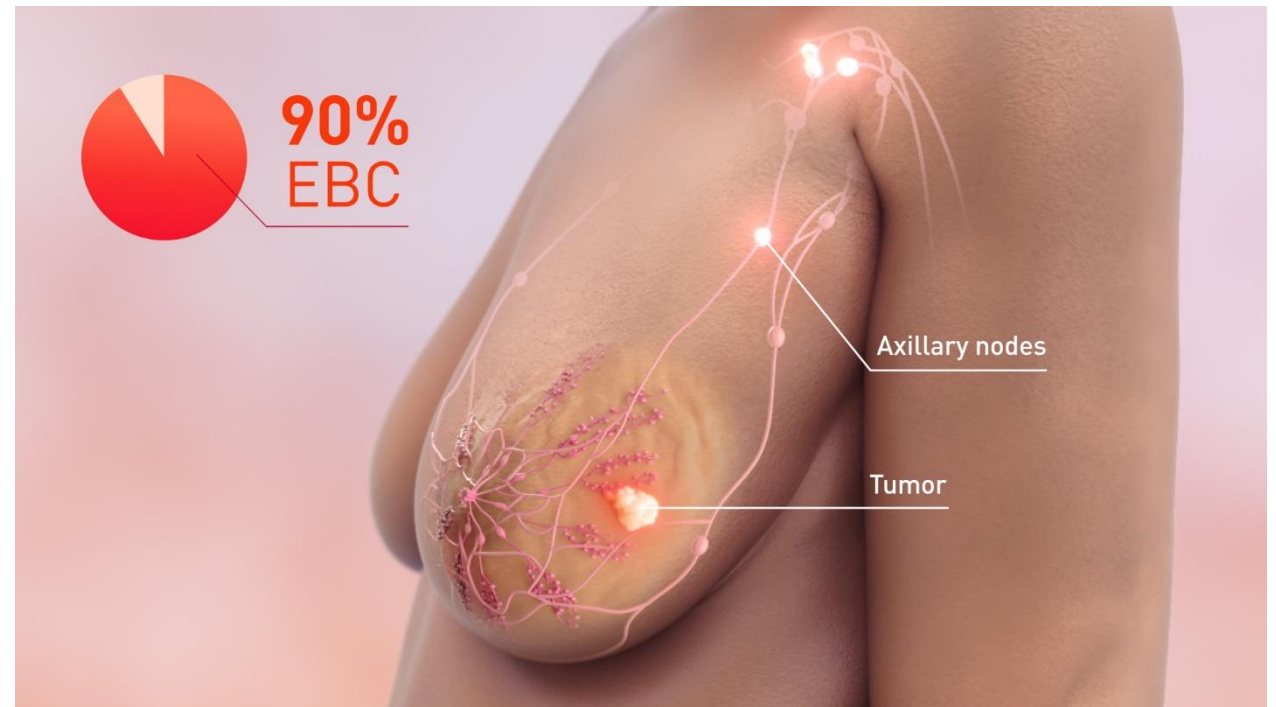


Early Breast Cancer: Introduction, Clinical Features, and Treatments

Breast Cancer: Introduction

- ◆ Breast cancer is the most commonly diagnosed cancer among women worldwide¹
- ◆ Among women, breast cancer accounts for one quarter of cancer cases and ~15% of all cancer deaths worldwide¹
- ◆ Women are at a ~100-fold greater risk of developing breast cancer than men²
- ◆ Early breast cancer, or EBC, is defined as disease confined within the breast and/or neighboring lymph nodes³
- ◆ Almost 90% of people with breast cancer are diagnosed with EBC⁴



EBC=early breast cancer.

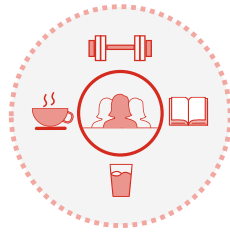
1. Sung H et al. *CA Cancer J Clin* 2021;71(3):209-249; 2. <https://www.cancer.org/cancer/breast-cancer-in-men/about/key-statistics.html>; 3. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/early-stage-breast-cancer>; 4. Howlader N et al. *J Natl Cancer Inst* 2014;106(5):dju055.

Breast Cancer: Risk Factors



Genetic and hereditary factors

BRCA1/2 mutations, family or personal history of breast or ovarian cancer¹



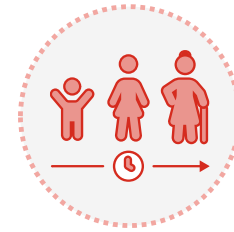
Lifestyle factors

Obesity after menopause, alcohol consumption, and lack of physical activity²



Hormone levels

Increased or abnormal estrogen and progesterone levels; postmenopausal replacement therapy^{3,4}



Age at menstruation/childbirth

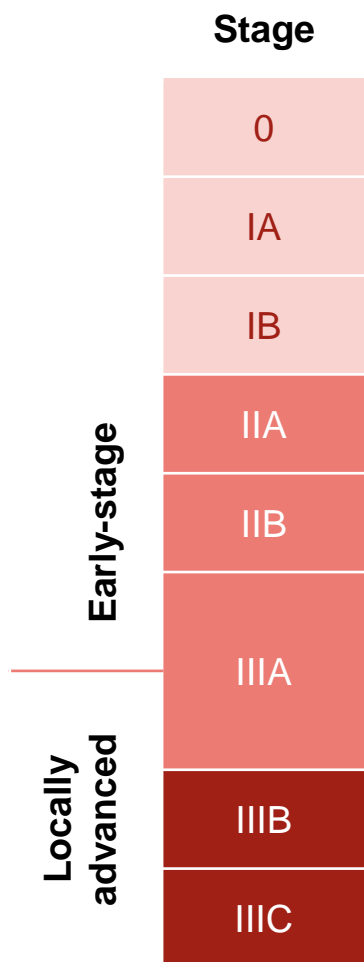
An early menarche or late menopause, giving birth at old age, and having fewer children⁵

Mammographic screening rates vary across geographical regions with developed countries reporting higher rates of screening⁶

BRCA1/2=breast cancer type 1/2 genes.

1. Bray F et al. *CA Cancer J Clin* 2018;68(6):394-424; 2. https://www.cdc.gov/cancer/breast/basic_info/risk_factors.htm; 3. <https://www.cancer.gov/about-cancer/causes-prevention/risk/hormones>; 4. <https://www.breastcancer.org/risk/factors/hrt>; 5. Sung H et al. *CA Cancer J Clin* 2021;71(3):209-249; 6. da Costa Vieira RA et al. *Clinics* 2017;72(4):244-253.

Early Breast Cancer Staging



- ◆ **Early breast cancer (EBC) can fall into the following stages according to the American Joint Committee on Cancer (AJCC) Tumor, Node, Metastasis (TNM) system^{1,2}**

Early-stage

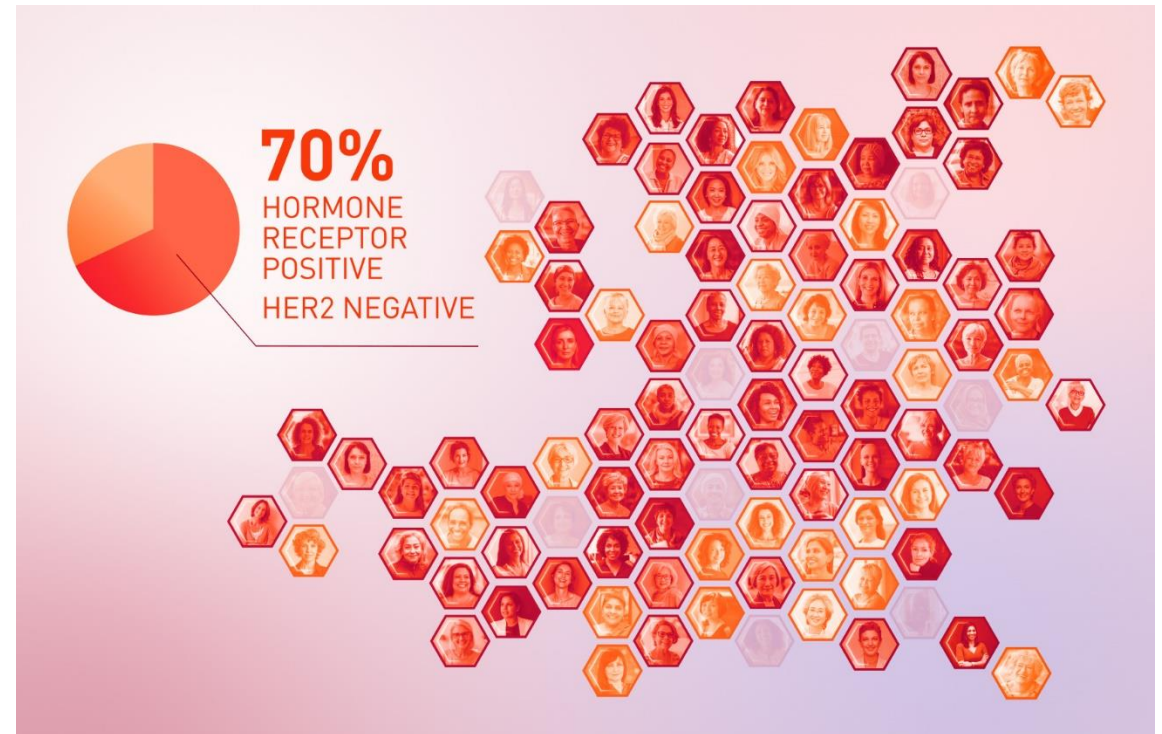
- **Stage 0:** Noninvasive *in situ* carcinoma found inside the ducts (Tis, N0, M0)^{1,2}
- **Stage IA:** Invasive breast cancer <2 cm in size, and have not spread to nearby lymph nodes (T1, N0, M0)^{1,2}
- **Stage IB:** Invasive breast cancer that has grown outside the ducts or lobules, ≤2 cm in size, that may have spread to nearby lymph nodes (T0/T1, N1mi, M0)^{1,2}
- **Stage IIA:** Invasive breast cancer that ≤2 cm in size with spreading to <4 lymph nodes, or ≤5 cm in size without spreading (T0/T1, N1, M0; or T2, N0, M0)^{1,2}
- **Stage IIB:** Invasive breast cancer that is 2-5 cm in size with spreading to <4 lymph nodes or >5 cm in size without spreading (T2, N1, M0; or T3, N0, M0)^{1,2}

Locally advanced

- **Stage IIIA:** Locally advanced breast cancer of any size without spread to chest wall or skin with spread to 4-9 nearby lymph nodes, or tumor more than 5 cm in size with spread to 1-3 nearby lymph nodes (T0/1/2/3, N2, M0; or T3, N1, M0)^{1,2}
- **Stage IIIB:** Locally advanced breast cancer with spread to chest wall or skin of breast and <9 axillary lymph nodes (T4, N0/1/2, M0)^{1,2}
- **Stage IIIC:** Locally advanced breast cancer spread to ≥10 axillary lymph nodes or lymph nodes near the collarbone or breastbone (T0/1/2/3/4, N3, M0)^{1,2}

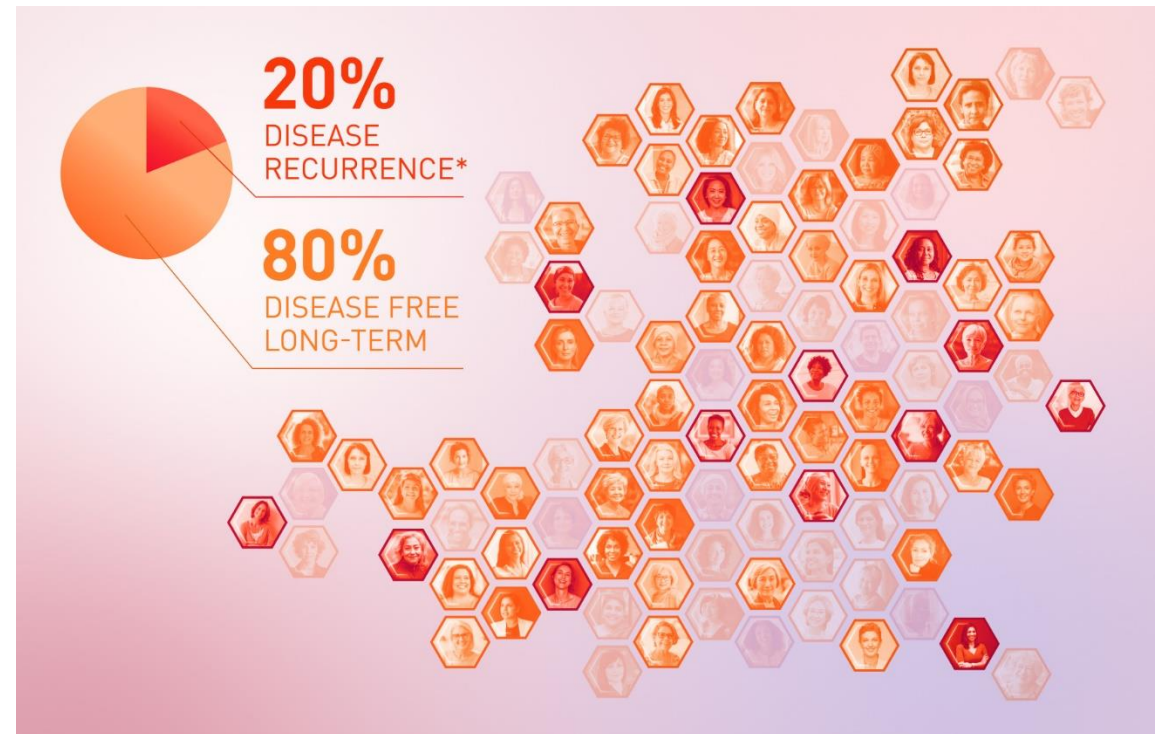
Early Breast Cancer Subtypes

- ◆ Approximately 70% of EBCs are characterized as hormone receptor (HR) positive (estrogen receptor [ER] and/or progesterone receptor [PR]) and human epidermal growth factor 2 (HER2) negative¹
- ◆ Other subtypes include¹
 - HR positive, HER2 positive
 - HR negative, HER2 positive
 - HR negative, HER2 negative (triple-negative)



Early Breast Cancer Subtypes

- ◆ About 80% of patients with EBC are disease-free in the long term¹
- ◆ However, approximately 20% will experience disease recurrence within 10 years¹ and may progress to incurable metastatic disease²

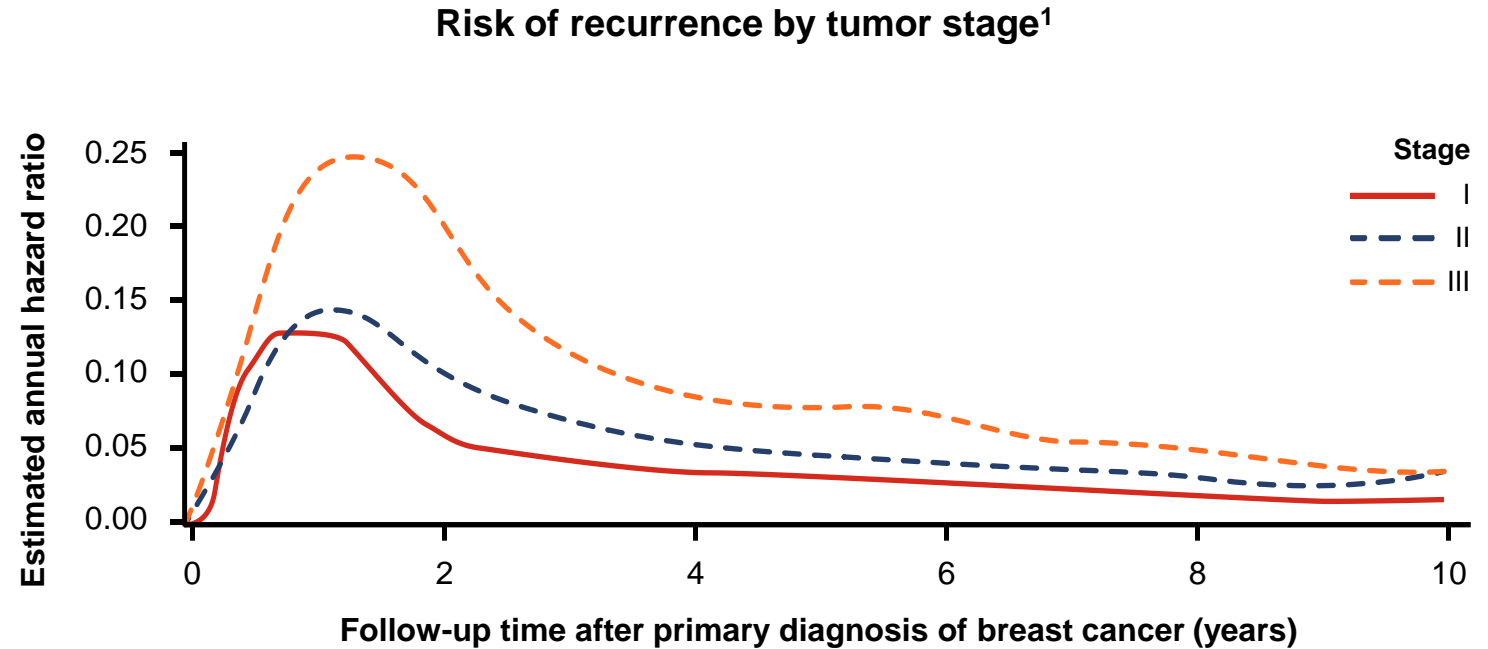


EBC=early breast cancer.

1. EBCTCG. *Lancet* 2015;386(10001):1341-1352; 2. Gerber B et al. *Dtsch Arztebl Int* 2010;107(6):85-91.

Early Breast Cancer Prognosis

- ◆ The risk of recurrence is highest in the first two years following diagnosis¹
- ◆ Critically, patients with disease recurrence have a worse prognosis and poorer overall outcomes²⁻⁴

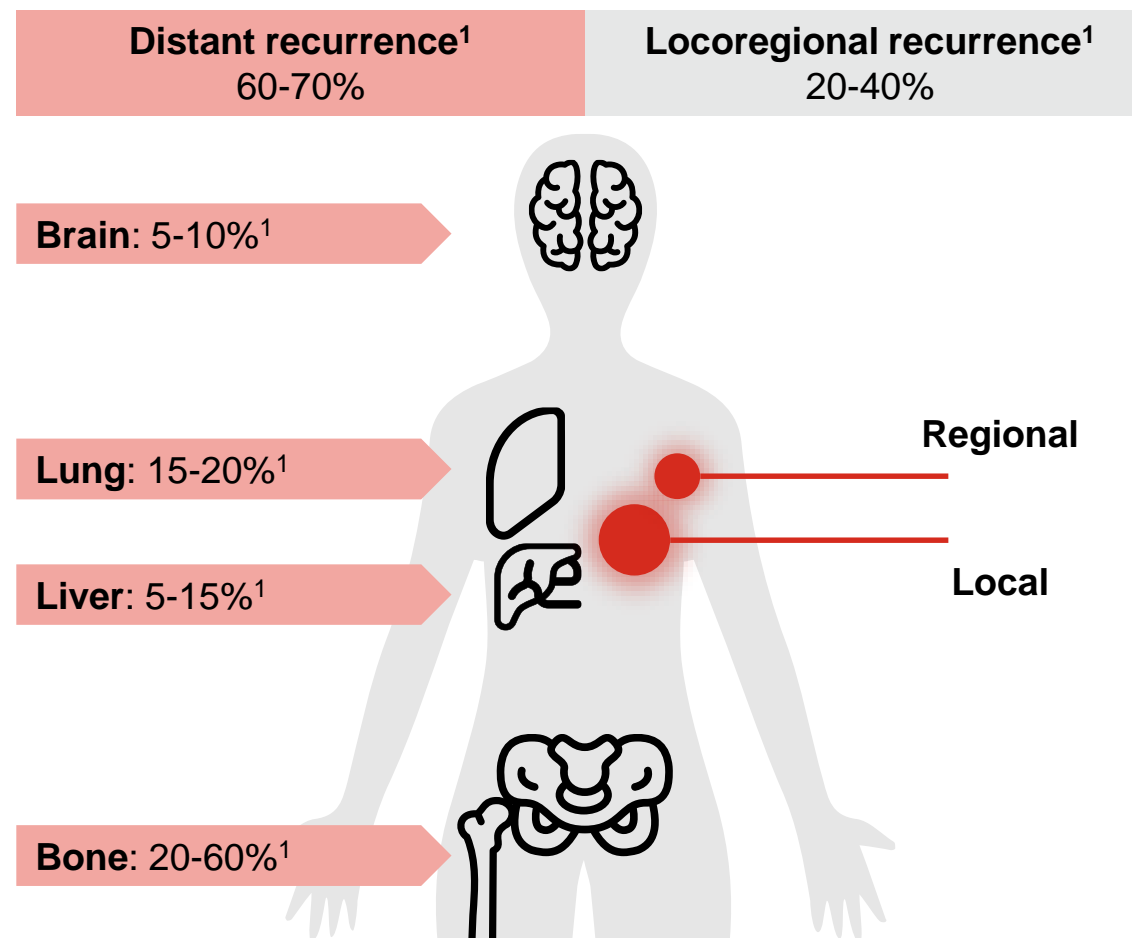


From Cheng et al., 2012.¹

1. Cheng L et al. *Cancer Epidemiol Biomark Prev* 2012;21(5):800-809; 2. EBCTCG. *Lancet* 2015;386(10001):1341-1352; 3. Johnston SRD et al. *J Clin Oncol* 2020;38(34):3987-3998; 4. Gerber B et al. *Dtsch Arztebl Int* 2010;107(6):85-91.

Early Breast Cancer Recurrence

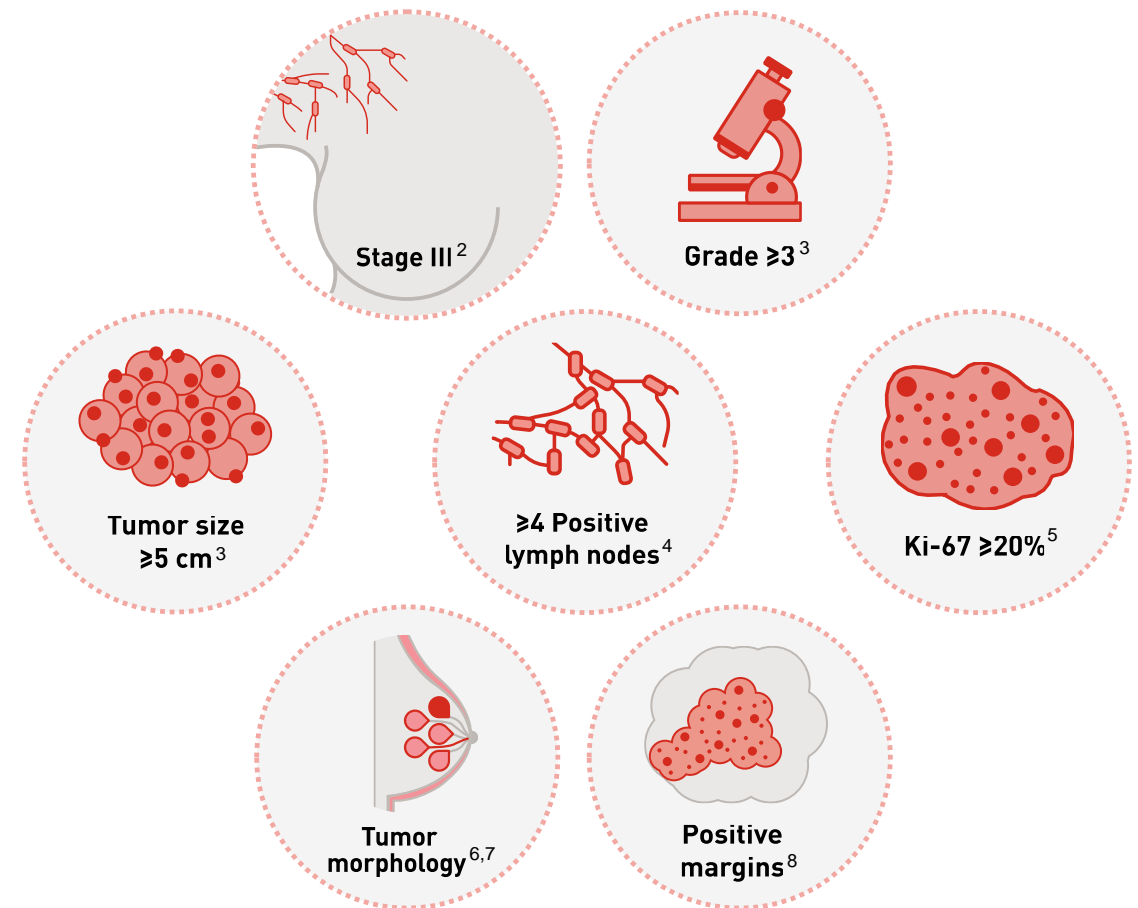
- ◆ There are three types of breast cancer recurrence¹
 - Local: Recurrence within the breast where the cancer originally started. Can also be in the skin and underlying tissues of the chest wall
 - Regional: Recurrence within the lymphatics near the affected breast
 - Distant: Recurrence in other parts of the body
- ◆ Most common sites are bone, liver, lungs, and brain¹
- ◆ Once distant recurrence has occurred, the disease remains largely incurable, but treatable²



1. Gerber B et al. *Dtsch Arztebl Int* 2010;107(6):85-89; 2. Cardoso F et al. *Ann Oncol* 2020;31(12):1623-1649.

Clinical Features of Early Breast Cancer Recurrence

- ◆ The portion of patients that experience recurrence or distant metastases in EBC is more likely to present high-risk clinical and/or pathologic features¹
- ◆ These features may include:
 - Tumor stage (III)²
 - Tumor grade (≥ 3)³
 - Tumor size (≥ 5 cm)³
 - Lymph node positivity (≥ 4 positive lymph nodes)⁴
 - Higher proliferation rates (Ki-67 “high” or $\geq 20\%$)⁵
 - Tumor morphology (ductal vs. lobular)^{6,7}
 - Positive margins⁸



EBC=early breast cancer.

1. Stuart-Harris R et al. *Breast (Online)* 2019;44:153-159; 2. Cheng L et al. *Cancer Epidemiol Biomark Prev* 2012;21(5):800-809; 3. Holleccek B et al. *BMC Cancer* 2019;19(1):520; 4. Pan H et al. *N Engl J Med* 2017;377(19):1836-1846; 5. Fasching PA et al. *Breast Cancer Res Treat* 2019;175(3):617-625; 6. Barroso-Sousa R et al. *Ther Adv Med Oncol* 2016;8(4):261-266; 7. Wasif N et al. *Ann Surg Oncol* 2010;17(7):1862-1869; 8. Freedman G et al. *Int J Radiat Oncol Biol Phys* 1999;44(5):1005-1015.

Early Breast Cancer Treatments

HR+, HER2- EBC treatment

Types of treatment (used alone or in combination)

- ◆ The goal of treatment in HR+, HER2- EBC is to eradicate the cancer and prevent disease recurrence¹
- ◆ The standard of care for HR+, HER2- EBC includes both locoregional therapies and systemic therapies¹

Locoregional treatment¹

- ◆ **Surgery**
- ◆ **Radiation therapy**

Systemic therapy (neoadjuvant/adjuvant therapy)¹

- | | | |
|---|--|--------------------------|
| ◆ Chemotherapy | ◆ Endocrine therapy | ◆ Bisphosphonates |
| <ul style="list-style-type: none">• Alkylating agents• Anthracyclines• Antimetabolites• Microtubule inhibitors | <ul style="list-style-type: none">• Selective estrogen receptor modulators• Aromatase inhibitors• Ovarian suppression/ablation | |

EBC=early breast cancer; HER2=human epidermal growth factor 2; HR=hormone receptor.

1. NCCN clinical practice guidelines in oncology: breast cancer V.5.2021. <https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1419>.

Summary: Early Breast Cancer

- ◆ Early breast cancer (EBC) is a disease confined within the breast and/or neighboring lymph nodes
- ◆ Nearly 90% of patients with breast cancer are diagnosed with EBC, of whom approximately 70% have cancers that are HR+, HER2-
- ◆ EBC is usually curable with about 80% of patients being disease free long-term. However, up to 20% of patients may experience disease recurrence
- ◆ The risk of recurrence is highest in the first two years following diagnosis
- ◆ Once distant recurrence has occurred, the disease remains largely incurable, but treatable
- ◆ A portion of patients that experience recurrence or distant metastases are more likely to present with high-risk clinicopathological features, such as high levels of Ki-67

