

## Breast cancer

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**Abstract** | Breast cancer is the most frequent malignancy in women worldwide and is curable in ~70–80% of patients with early-stage, non-metastatic disease. Advanced breast cancer with distant organ metastases is considered incurable with currently available therapies. On the molecular level, breast cancer is a heterogeneous disease; molecular features include activation of human epidermal growth factor receptor 2 (HER2, encoded by *ERBB2*), activation of hormone receptors (oestrogen receptor and progesterone receptor) and/or *BRCA* mutations. Treatment strategies differ according to molecular subtype. Management of breast cancer is multidisciplinary; it includes locoregional (surgery and radiation therapy) and systemic therapy approaches. Systemic therapies include endocrine therapy for hormone receptor-positive disease, chemotherapy, anti-HER2 therapy for HER2-positive disease, bone stabilizing agents, poly(ADP-ribose) polymerase inhibitors for *BRCA* mutation carriers and, quite recently, immunotherapy. Future therapeutic concepts in breast cancer aim at individualization of therapy as well as at treatment de-escalation and escalation based on tumour biology and early therapy response. Next to further treatment innovations, equal worldwide access to therapeutic advances remains the global challenge in breast cancer care for the future.

Breast cancer is the most frequent malignancy in women and is a heterogeneous disease on the molecular level. Over the past 10–15 years, treatment concepts have evolved to take this heterogeneity into account, with emphasis being placed on more biologically-directed therapies and treatment de-escalation to reduce the adverse effects of treatment. Despite the inherent molecular heterogeneity, which is a driving principle of modern-day treatments, some features such as the impact of locoregional tumour burden or metastatic patterns are shared and influence therapy. Early breast cancer — that is, cancer that is contained in the breast or that has only spread to the axillary lymph nodes — is considered curable. Improvements in multimodal therapy have led to increasing chances for cure in ~70–80% of patients. By contrast, advanced (metastatic) disease is not considered curable using currently available therapeutic options. However, advanced breast cancer is a treatable disease, for which the main goals of therapy are to prolong survival and control symptoms with low treatment-associated toxicity to maintain or improve quality of life (that is, improved quality-adjusted life expectancy).

The two major pillars of breast cancer management are locoregional treatment and systemic therapy; the histological and molecular characteristics of breast cancer largely influence treatment decisions. The molecular

alterations that drive breast carcinogenesis are many, and several classifications have been developed to group tumours accordingly. The intrinsic classification of Perou and Sorlie<sup>1</sup>, reported in 2000, distinguished four subtypes of breast cancer: luminal A and luminal B (expressing the oestrogen receptor (ER)), basal-like and human epidermal growth factor receptor 2 (HER2)-enriched (without ER expression). This classification shifted clinical management of breast cancer from being based on tumour burden to biology-centred approaches. Currently, clinical practice typically uses a surrogate classification of five subtypes on the basis of histological and molecular characteristics (FIG. 1). Tumours expressing ER and/or progesterone receptor (PR) are considered hormone receptor-positive breast cancers, whereas tumours that do not express ER, PR or HER2 are triple-negative breast cancer (TNBC). Importantly, treatment by a specialized multidisciplinary team improves survival and quality of life for patients with early and metastatic breast cancer, as does treatment according to high-quality guidelines. Establishment of specialized breast cancer centres is a major priority worldwide, and is supported by the European Parliament<sup>2</sup>.

As breast cancer is a global problem, major emphasis needs to be put on diminishing worldwide disparities in access to diagnosis, multimodal treatment and novel drugs. In this Primer, we provide state-of-the-art

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