PRIMER

Breast cancer

Nadia Harbeck^{*} *, Frédérique Penault-Llorca², Javier Cortes^{3,4}, Michael Cnant⁵, Nehmat Houssami⁸, Phillip Poortmans^{3,8}, Kathryn Ruddy⁸, Janice Tsang¹⁰ and Fatima Cardoso¹¹

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 ER682), 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 beterogeneity, 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 therany 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 engrectamey's.

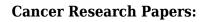
The two major pillars of breast cancer management are locoregional treatment and systemic therapy; the histological and molecular characteristics of breast cancer largely influence treatment decisions. The molecular alterations that drive breast carcinogenesis are many. and several classifications have been developed to group turnours accordingly. The intrinsic classification of Perou and Sorlie', reported in 2000, distinguished four subtypes of breast cancer: luminal A and luminal B (expressing the oestrogen receptor (ER)), basal-like and buman epidermal growth factor receptor 2 (HER2)enriched (without ER expression). This classification shifted clinical management of breast cancer from being based on turnour 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]. Turnours 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 triplenegative 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'.

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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Table of Contents Cancer Research Papers

- 1. Understanding the eBook Cancer Research Papers
 - The Rise of Digital Reading Cancer Research Papers
 - Advantages of eBooks Over Traditional Books
- 2. Identifying Cancer Research Papers
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
- 3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Cancer Research Papers
 - User-Friendly Interface
- 4. Exploring eBook Recommendations from Cancer Research Papers
 - Personalized Recommendations

- Cancer Research Papers User Reviews and Ratings
- Cancer Research Papers and Bestseller Lists
- 5. Accessing Cancer Research Papers Free and Paid eBooks
 - Cancer Research Papers Public Domain eBooks
 - Cancer Research Papers eBook Subscription Services
 - Cancer Research Papers Budget-Friendly Options
- 6. Navigating Cancer Research Papers eBook Formats
 - o ePub, PDF, MOBI, and More
 - Cancer Research Papers Compatibility with Devices
 - Cancer Research Papers Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - o Adjustable Fonts and Text Sizes of Cancer Research Papers
 - Highlighting and Note-Taking Cancer Research Papers
 - Interactive Elements Cancer Research Papers
- 8. Staying Engaged with Cancer Research Papers
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Cancer Research Papers
- 9. Balancing eBooks and Physical Books Cancer Research Papers
 - ∘ Benefits of a Digital Library
 - Creating a Diverse Reading Collection Cancer Research Papers
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Cancer Research Papers
 - Setting Reading Goals Cancer Research Papers
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Cancer Research Papers
 - Fact-Checking eBook Content of Cancer Research Papers

- Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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