Precision medicine in breast cancer (Review)

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Abstract. Precision medicine in breast cancer is a revolutionary approach that customizes diagnosis and treatment based on individual and tumor characteristics, departing from the traditional one-size-fits-all approach. Breast cancer is diverse, with various subtypes driven by distinct genetic mutations. Understanding this diversity is crucial for tailored treatment strategies that target specific vulnerabilities in each tumor. Genetic testing, particularly for mutations in breast cancer gene (BRCA) DNA repair-associated genes, helps assess hereditary risks and influences treatment decisions. Molecular subtyping guides personalized treatments, such as hormonal therapies for receptor-positive tumors and human epidermal growth factor receptor 2 (HER2)-targeted treatments. Targeted therapies, including those for HER2-positive and hormone receptor-positive breast cancers, offer more effective and precise interventions. Immunotherapy, especially checkpoint inhibitors, shows promise, particularly in certain subtypes such as triple-negative breast cancer, with ongoing research aiming to broaden its effectiveness. Integration of big data and artificial intelligence enhances personalized treatment strategies, while liquid biopsies provide real-time insights into tumor dynamics, aiding in treatment monitoring and modification. Challenges persist, including accessibility and tumor complexity, but emerging technologies and precision prevention offer hope for improved outcomes. Ultimately, precision medicine aims to optimize treatment efficacy, minimize adverse effects and enhance the quality of life for patients with breast cancer.

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1. Introduction

Precision medicine in breast cancer stands at the forefront of transformative healthcare, reshaping the landscape of diagnosis, treatment, and management strategies. This innovative approach, tailored to the individual characteristics of both the patient and their tumor, marks a paradigm shift from traditional one-size-fits-all cancer therapies to a more personalized, targeted and effective treatment regimen (1,2).

Breast cancer remains a major global health concern, being the most common cancer type in women worldwide. According to the World Health Organization, in 2020, there were ~2.3 million new cases and 685,000 deaths globally. In the United States alone, it is estimated that ~1 in 8 women (13%) will develop invasive breast cancer over the course of their lifetime (3). Despite advancements in early detection and treatment, the heterogeneous nature of breast cancer poses significant challenges in achieving optimal patient outcomes. This heterogeneity encompasses various subtypes driven by distinct genetic mutations, molecular profiles and cellular characteristics, which significantly influence the behavior of tumors and their response to treatment (4).

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Genetic testing, particularly for BRCA DNA repair associated 1 (BRCA1) and BRCA2 mutations, plays a critical role in assessing hereditary risk factors and guiding treatment decisions. Individuals carrying these mutations have a higher risk of developing breast cancer, necessitating personalized surveillance and preventive strategies (5). The classification of breast cancer into subtypes such as hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-positive and triple-negative breast cancer (TNBC) allows for more precise treatment strategies. Each subtype responds differently to therapies, emphasizing the need for tailored treatment plans (6-8).

Advances in targeted therapies, including HER2 inhibitors and hormonal treatments, have significantly improved outcomes for patients with specific subtypes of breast cancer. These therapies offer a more effective approach by directly targeting the molecular abnormalities driving tumor growth. Emerging treatments like immune checkpoint inhibitors show promise, particularly in TNBC, and ongoing research aims to expand the applicability of immunotherapy across various breast cancer subtypes (7,9).

Additionally, the use of big data analytics and artificial intelligence (AI) enhances our understanding of breast cancer biology, facilitating the development of predictive models and personalized treatment strategies (10). Non-invasive liquid biopsies provide real-time insights into tumor dynamics, enabling continuous monitoring and timely adjustments in therapy (11).

While significant progress has been made, challenges remain, including the accessibility of advanced medical technologies, managing tumor heterogeneity and addressing acquired resistance to therapies. Continued research and innovation are essential to overcoming these barriers and achieving the full potential of precision medicine in breast cancer. By leveraging the advancements in genomics, targeted therapies, immunotherapy, data analytics and innovative diagnostics, precision medicine aims to optimize treatment efficacy, minimize adverse effects and ultimately enhance the quality of life for individuals affected by breast cancer (12,13).

2. Understanding breast cancer diversity

The diversity within breast cancer is a pivotal aspect that shapes its behavior and determines treatment responses and patient outcomes. It's not a singular disease but a complex spectrum comprising various subtypes, each exhibiting unique genetic, molecular and cellular characteristics. This inherent heterogeneity profoundly influences how tumors behave and how they respond to different treatments, and ultimately impacts patient prognosis (14,15).

The different subtypes of breast cancer arise from distinct genetic mutations or alterations within the DNA of breast cells. These alterations drive the growth and behavior of the tumor. For instance, the presence or absence of hormone receptors [estrogen receptors (ER), progesterone receptors (PR)] and the overexpression of the HER2/neu gene play crucial roles in defining specific breast cancer subtypes (16,17).

The recognition of these variations in breast cancer subtypes has given rise to the paradigm of precision medicine. Instead of a universal method, precision medicine recognizes and embraces the variations within breast cancer. It emphasizes the need for tailored and personalized treatment strategies that account for the unique characteristics of each patient's tumor (18,19).

This shift in approach is significant, as it acknowledges that what works for one subtype of breast cancer may not be as effective for another. For instance, hormone receptor-positive breast cancers respond well to hormonal therapies that target these receptors, while HER2-positive tumors benefit from therapies specifically designed to inhibit the HER2 protein (20).

Furthermore, this diversity influences the behavior of tumors, impacting their aggressiveness, growth rates, likelihood of spreading (metastasis) and response to various treatments. Certain subtypes may be more aggressive and fast-growing, while others may respond better to certain therapies but poorly to others.

Appreciating and understanding this diversity is fundamental to developing targeted therapies. By identifying specific genetic or molecular alterations within each subtype, oncologists can tailor treatments to attack these specific vulnerabilities in the tumor. This approach leads to more effective treatments that precisely target the unique characteristics of a patient's cancer while minimizing side effects (21,22).

3. Genetic insights and risk assessment

Genetic testing has become an integral part of precision medicine in the realm of breast cancer. This innovative approach involves the examination of specific genes, notably the breast cancer genes BRCA1 and BRCA2, to uncover potential mutations or alterations that significantly contribute to a heightened risk of developing breast cancer (23).

However, in addition to the geneticist's perspective, it is crucial to incorporate insights from medical professionals and patients to provide a comprehensive view of precision medicine. Medical professionals can offer practical insights into the clinical implementation and ethical considerations of precision medicine, while patients' experiences and preferences are essential for tailoring treatments that improve their quality of life (24,25). Furthermore, the concept of precision medicine, which involves calculating personal risks based on genetic data in the context of a referential population, can be prone to errors. These errors may arise from the complexity of genetic information, variability in genetic databases and potential misinterpretations, particularly when dealing with rare or poorly understood genetic variants (21).

The discovery of mutations within the BRCA1 and BRCA2 genes has profound implications, particularly in assessing hereditary risk factors associated with breast cancer. Individuals carrying mutations in these genes have a notably higher risk of developing breast and ovarian cancers compared to the general population. This knowledge has revolutionized risk assessment, enabling healthcare professionals to identify individuals who may be predisposed to these hereditary forms of cancer (26,27).

Genetic testing offers a personalized understanding of an individual's risk profile. For those identified as carrying BRCA mutations, personalized risk assessment becomes crucial. It not only aids in understanding their likelihood of developing breast cancer but also extends to assessing the risk of other associated cancers, such as ovarian cancer. Armed with

this knowledge, patients and healthcare providers can make well-considered choices regarding proactive steps to handle and reduce these risks.

Increased surveillance, such as more frequent screenings or specific imaging modalities, is often recommended for individuals identified as having a higher genetic predisposition to breast cancer. In addition, risk-reducing surgeries, such as prophylactic mastectomy or oophorectomy, may be considered preventive measures in high-risk individuals, significantly reducing the chances of developing breast or ovarian cancer (24,25).

Furthermore, genetic insights are not limited to risk assessment alone; they also play a pivotal role in guiding treatment decisions. In cases where a patient's tumor exhibits specific genetic mutations or alterations, this information can influence the selection of targeted therapies. For instance, individuals with BRCA mutations may benefit from specific drugs or treatments that target these genetic vulnerabilities within the tumor, leading to more effective and tailored treatment plans (28,29).

Understanding an individual's genetic predisposition to breast cancer is a cornerstone of precision medicine. It not only informs personalized risk assessment but also guides treatment strategies, empowering patients and healthcare providers to make informed decisions about proactive measures and tailored treatments. This personalized approach significantly enhances the efficacy of interventions and improves patient outcomes in the realm of breast cancer management (30,31).

4. Genomic profiling and molecular subtyping

Advancements in genomic profiling techniques have ushered in a new era of understanding the intricacies of breast cancer biology. These sophisticated molecular analysis methods delve deep into the genetic makeup of tumors, unraveling specific genetic mutations, alterations or expression patterns that underpin the disease's development and progression (32).

One of the key contributions of genomic profiling is the ability to molecularly subtype breast cancers. These subtypes are determined by analyzing various molecular characteristics present in the tumor. Hormone receptor status, primarily the presence of ER and PR, serves as a fundamental classification criterion. Tumors that express these receptors (ER-positive or PR-positive) respond differently to treatments compared to those lacking these receptors (ER-negative or PR-negative) (33,34).

In addition, the expression of HER2 represents another crucial molecular marker. HER2-positive tumors overexpress the HER2 protein, leading to aggressive tumor behavior. Identification of the HER2 status is pivotal, as it influences treatment decisions, such as targeted therapies like trastuzumab, specifically designed to inhibit HER2 (35-37).

Furthermore, gene expression profiling techniques, such as the Prosigna Breast Cancer Prognostic Gene Signature (PAM50) assay, have emerged as valuable tools in molecular subtyping. The PAM50 assay evaluates the expression of a panel of genes within the tumor, enabling the categorization of breast cancers into distinct molecular subgroups. These subtypes, such as Luminal A, Luminal B, HER2-enriched and TNBC, provide deeper insights into tumor behavior and response to treatments (38,39).

Molecular subtyping offers a refined understanding of breast cancer heterogeneity. It allows oncologists to categorize tumors into specific subgroups based on their unique molecular characteristics, guiding tailored therapeutic interventions. For instance, hormone receptor-positive tumors typically respond well to hormonal therapies, while HER2-positive tumors benefit from HER2-targeted treatments. Conversely, TNBCs, lacking these receptors, often require different approaches, such as chemotherapy (40).

This molecular categorization aids in personalized treatment planning, facilitating the selection of therapies that precisely target the biological characteristics of each subtype. By aligning treatments with the molecular profile of the tumor, clinicians can optimize treatment efficacy while minimizing unnecessary side effects (41).

5. Targeted therapies and personalized treatment

The emergence of targeted therapies marks a groundbreaking advancement in the field of breast cancer management. These therapies represent a sophisticated approach that aims to target precisely the underlying molecular abnormalities driving the growth and spread of tumors.

One of the remarkable success stories in targeted therapies is the development of treatments specifically designed for HER2-positive breast cancer. HER2, a protein overexpressed in certain breast cancers, plays a crucial role in promoting aggressive tumor behavior. Targeted agents like trastuzumab and pertuzumab are monoclonal antibodies that act by binding to the HER2 receptor, inhibiting its signaling pathways and effectively slowing down tumor growth. These therapies have transformed the outlook for patients with HER2-positive breast cancer, significantly improving survival rates and reducing the risk of recurrence (42,43).

Another pivotal area of targeted therapy lies in addressing hormone receptor-positive breast cancers. Hormone receptor-positive tumors, particularly those expressing ER, rely on hormone signaling pathways for their growth. Targeted hormonal therapies aim to disrupt these pathways, thereby impeding tumor proliferation. Aromatase inhibitors and selective ER modulators (SERMs) are among the tailored treatments used for this subtype. Aromatase inhibitors, for example, inhibit the production of estrogen in postmenopausal women, while SERMs like tamoxifen block estrogen from binding to receptors in breast cells, effectively hindering tumor growth (44,45).

These targeted therapies exemplify the shift towards personalized treatment approaches in breast cancer. By focusing on the specific molecular characteristics of each subtype, these therapies offer more effective and tailored interventions. This tailored method not only boosts the effectiveness of treatments but also reduces negative impacts on healthy tissues, ultimately enhancing the life quality of patients receiving these therapies (Fig. 1) (46).

6. Immunotherapy and its promise

Immunotherapy has emerged as a promising frontier in the realm of breast cancer treatment, heralding a novel approach that harnesses the body's immune system to combat cancer
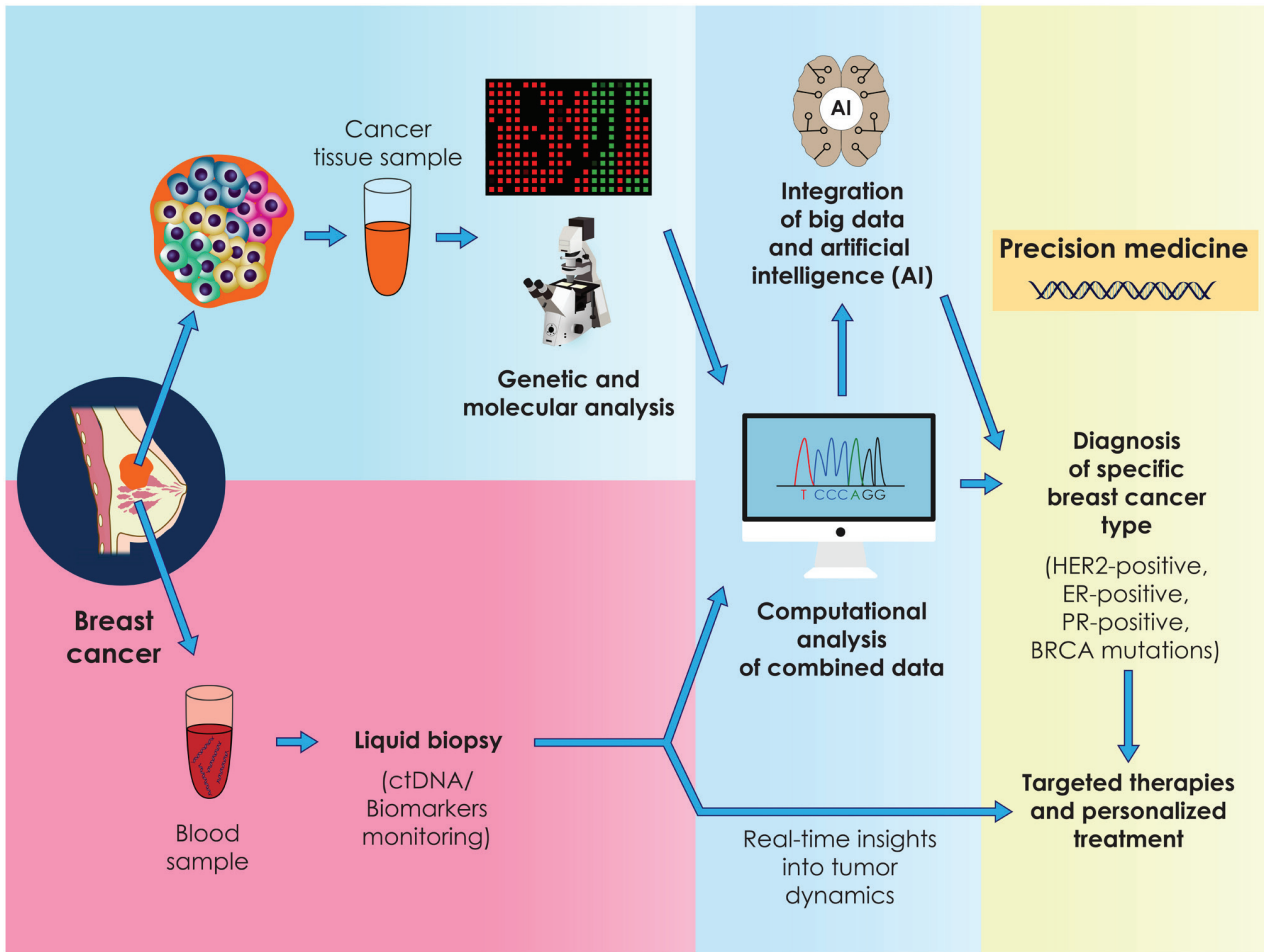
Figure 1. Suggested model of application of precision medicine in breast cancer. BRCA, BRCA DNA repair associated; HER2, human epidermal growth factor receptor 2; ER, estrogen receptor; PR, progesterone receptor; ctDNA, circulating tumor DNA.

cells. At the forefront of this innovative approach are immune checkpoint inhibitors, such as pembrolizumab and nivolumab, which have shown significant potential in transforming cancer therapy. These inhibitors function by blocking proteins like programmed cell death 1/programmed cell death ligand 1 (PD-L1) and cytotoxic T-lymphocyte associated protein 4, which tumors use to evade immune detection. By inhibiting these checkpoints, these therapies enhance the immune system's ability to recognize and attack cancer cells. The effectiveness of these inhibitors can be significantly improved through precision medicine approaches that involve genetic and molecular profiling to identify biomarkers indicative of a likely response to immunotherapy (47-49).

While the efficacy of immunotherapy, particularly checkpoint inhibitors, has been more conspicuous in certain subsets of breast cancer, such as TNBC, ongoing research endeavors aim to expand its scope across various breast cancer subtypes. TNBC, characterized by the absence of hormone receptors and HER2 expression, has shown particular promise in responding to immunotherapy due to its heightened immune response and increased presence of immune cells within the tumor microenvironment (50,51).

However, the efficacy of immunotherapy in other breast cancer subtypes, such as hormone receptor-positive or HER2-positive cancers, has been more modest. Researchers are actively exploring combination therapies that combine immunotherapy with other treatment modalities, including chemotherapy, targeted therapies or other immune-modulating agents. These combinations aim to augment the immune system's response and enhance the effectiveness of immunotherapy across a broader spectrum of patients with breast cancer (52,53).

Furthermore, ongoing efforts to identify predictive biomarkers play a crucial role in refining patient selection for immunotherapy. Biomarkers, such as PD-L1 expression on tumor cells or tumor-infiltrating lymphocytes, serve as indicators of potential responsiveness to checkpoint inhibitors. Incorporating these biomarkers into clinical decision-making helps identify patients who are more likely to benefit from immunotherapy, ensuring a more tailored and effective treatment approach.

The evolving landscape of immunotherapy in breast cancer treatment holds promise for advancing therapeutic options. While the current success has been more pronounced in specific subtypes, ongoing research endeavors aim to broaden its applicability across a wider spectrum of patients with breast cancer. Through combination therapies, biomarker identification and ongoing clinical trials, the goal is to optimize the efficacy of immunotherapy and integrate it into the paradigm of personalized breast cancer treatment (54,55).

7. Integration of big data and AI

The integration of big data analytics and AI has heralded a transformative era in precision medicine, particularly in the context of breast cancer research and treatment. Incorporating multi-omics approaches, which include genomics, proteomics, metabolomics and transcriptomics, can provide a more comprehensive understanding of cancer biology. This multi-faceted approach allows for a deeper insight into tumor heterogeneity and can lead to more effective and personalized treatment strategies (56,57).

These cutting-edge technologies empower researchers and clinicians to navigate and analyze vast and intricate datasets encompassing genetic information, treatment responses, patient outcomes and a multitude of clinical variables (58).

At the core of this integration lies the capacity to process and derive insights from immense volumes of diverse data. Big data analytics, leveraging advanced computational techniques, sifts through this wealth of information to identify subtle patterns, correlations and associations that may elude traditional analytical methods. Within the realm of breast cancer, these datasets include genetic profiles obtained through genomic sequencing, molecular data characterizing tumor subtypes, treatment history, patient demographics and clinical outcomes (59).

AI, particularly machine learning algorithms, has a significant role in decoding this complex data landscape. These algorithms possess the capacity to learn and adapt autonomously, recognizing intricate relationships and deciphering patterns within the datasets. By processing this information, AI algorithms can generate predictive models that aid clinicians in crafting well-informed choices customized for each patient. For instance, these models can predict treatment responses, anticipate potential side effects, forecast disease progression or identify personalized therapeutic strategies based on a patient's unique genetic makeup and clinical profile (60).

In the context of breast cancer, AI algorithms, particularly machine learning, can process and analyze vast datasets comprising genetic information, clinical records and treatment outcomes, uncovering patterns and insights that are beyond human capability. These insights can inform personalized treatment strategies, predicting which therapies will be most effective for individual patients based on their unique genetic and molecular profiles. Future advancements in AI and big data analytics will continue to refine these approaches, enabling more precise and effective cancer treatments. The ability to continuously learn and adapt from new data will allow AI to stay at the forefront of precision medicine, ultimately leading to better patient outcomes (61).

Furthermore, the ongoing evolution of these technologies continues to refine their capabilities. With ongoing progression in machine learning algorithms and data analytics, the precision and accuracy of predictive models are improving. Integration with real-time patient data from diverse sources further enhances the depth and breadth of insights generated by these AI-driven approaches. However, it is important to note that, while the potential of big data and AI in breast cancer research and treatment is promising, challenges remain. Issues related to data privacy, data standardization and the need for validation and clinical translation of AI-generated insights pose significant hurdles that need to be addressed (62).

8. Liquid biopsies and real-time monitoring

Liquid biopsies represent a groundbreaking, non-invasive technique in cancer diagnosis and surveillance, providing exceptional real-time understanding of tumor genetics and behavior. This innovative approach involves analyzing circulating tumor DNA (ctDNA) or specific biomarkers present in blood samples, presenting a promising avenue for monitoring treatment response, detecting potential resistance mechanisms and guiding timely adjustments in therapy (63,64).

One of the primary advantages of liquid biopsies lies in their non-invasive nature. Unlike traditional tissue biopsies, which involve invasive procedures to extract tissue samples from the tumor site, liquid biopsies utilize blood samples. These blood samples contain circulating tumor components, such as ctDNA, exosomes, circulating tumor cells and other tumor-specific biomarkers shed by the tumor into the bloodstream.

The analysis of these components provides a dynamic and comprehensive view of the tumor's genetic makeup and behavior. By examining ctDNA, which comprises fragments of tumor DNA released into the bloodstream, liquid biopsies can reveal specific genetic alterations, mutations or genomic rearrangements present in the tumor. This information is invaluable in understanding the tumor's heterogeneity, predicting treatment responses and identifying potential resistance mechanisms that may emerge during the course of treatment (65,66).

Furthermore, the real-time nature of liquid biopsies allows for continuous monitoring of the tumor's status throughout the treatment journey. These tests offer the ability to track changes in the tumor profile over time, enabling clinicians to promptly detect any alterations in the tumor's genetic landscape. This capability is crucial in identifying early signs of treatment response or disease progression and facilitating timely interventions and adjustments in therapy regimens (67).

Liquid biopsies hold immense promise in various facets of cancer management, including breast cancer. In the context of breast cancer treatment, these tests enable clinicians to monitor the effectiveness of targeted therapies or chemotherapy, assess the emergence of treatment resistance and make informed decisions regarding treatment modifications or switches to alternative therapies.

In addition, liquid biopsies have the potential to revolutionize post-treatment surveillance. They can detect minimal residual disease or early signs of recurrence more sensitively than conventional imaging techniques, allowing for earlier intervention and potentially improving patient outcomes.

However, while liquid biopsies offer tremendous potential, several challenges remain. Standardization of methodologies, optimization of sensitivity and specificity, and validation of their clinical utility in large-scale studies are essential to ensuring their widespread adoption in routine clinical practice. Overcoming these challenges will further enhance the role of liquid biopsies as a crucial tool in the armamentarium of cancer diagnostics and monitoring, shaping a more personalized and dynamic approach to cancer care (68-70).

9. Challenges and future directions

Despite the remarkable strides, challenges persist in implementing precision medicine universally. One of the primary obstacles is ensuring equitable access to these advanced medical technologies. Socioeconomic disparities, geographic limitations and variations in healthcare infrastructure can lead to unequal access to genomic testing and personalized treatments. Addressing these barriers is crucial to ensure that the benefits of precision medicine are available to all populations, regardless of their socioeconomic status or geographic location (69,70). Access to advanced genomic testing, targeted therapies and specialized treatments may be limited in certain healthcare settings or regions. In addition, tumor heterogeneity, acquired resistance to targeted therapies and the evolving complexity of cancer biology pose ongoing challenges that necessitate continued research and innovation (69).

The future of precision medicine for breast cancer holds immense promise. Progressions in technology, such as single-cell sequencing, spatial genomics and multi-omics approaches, offer a deeper understanding of tumor heterogeneity and evolution. Integrating diverse treatment modalities, including targeted therapies, immunotherapy and emerging novel agents, in a personalized approach based on comprehensive molecular profiling holds potential to further improve patient outcomes (70).

Furthermore, precision prevention emerges as a significant aspect, focusing on identifying high-risk individuals through genetic screening and implementing personalized interventions to prevent breast cancer development or detect it at an early, more curable stage (56). Another future promising field of precision medicine recommends radiogenomics that combines genomic profiles and particular imaging features of every individual that have been recognized and show promising results in the diagnosis and prognosis of breast cancer (71).

In conclusion, precision medicine in breast cancer epitomizes a tailored, patient-centric approach that leverages the advancements in genomics, targeted therapies, immunotherapy, data analytics and innovative diagnostics. By harnessing the power of personalized medicine, the goal is to optimize treatment efficacy, minimize adverse effects, and ultimately enhance the quality of life for individuals affected by breast cancer. However, achieving widespread implementation requires concerted efforts in research, accessibility, healthcare infrastructure and interdisciplinary collaborations to fully harness the potential of precision medicine in combating breast cancer.

Availability of data and materials

Not applicable.

Authors' contributions

PP and VEG conceptualized the study. PP, VEG, PVD, ET, AN, ACL, GCZ, DAS, NK and GET made substantial contributions to data interpretation and analysis and wrote and prepared the draft of the manuscript. DAS and VEG analyzed the data and provided critical revisions. All authors have read and approved the final manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

DAS is the Editor-in-Chief for the journal, but had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article. The other authors declare that they have no competing interests.

Use of AI tools

During the preparation of this work, the AI tool Chat GPT was used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the AI tool as necessary, taking full responsibility for the ultimate content of the present manuscript.

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