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Breast Cancer: Big Challenge for Women

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1. Introduction

Half of the world's population is female that brings off springs into the world. she keeps it in her stomach for nine months and breastfeeds it after birth and world keeps growing. Now a days, breast cancer has emerged as a challenge in the world. So, this is necessary to save women from the breast cancer. It is very necessary for our society.

The Global prevalence of cancer is a critical public health issue, with rising incidence and mortality rates observed in both economically developing and developed nations [1,2]. Among cancers, breast cancer (BC) stands out as the most commonly diagnosed type and a leading cause of cancer-related deaths among females [2]. It constitutes 23% of total cancer cases and 14% of cancer-related deaths, even becoming the primary cause of female cancer mortality in economically developing regions [2]. Environmental factors and dietary habits play a major role in BC development, with additional contributors such as virus-mediated genetic changes [3].

Cancer's development involves the disruption of various signalling pathways, resulting in heightened cell proliferation, survival, and resistance to anticancer drugs [4]. In BC, the key dysregulations are the deactivation of tumour suppressor genes and the excessive activation of proto-oncogenes. Breast cancer encompasses a diverse group of neoplasms originating from epithelial cells, presenting a complex challenge to the fields of medicine and immunology [5]. Consequently, there's a clear need for more effective therapies to combat these malignancies.

Current FDA-approved treatments for BC, including fulvestrant, lapatinib, eribulin mesylate, pertuzumab, and everolimus, have faced limitations due to drug resistance. Thus, there's a requirement for alternative treatments to offer a foolproof solution against BC. Despite significant research progress in cancer treatment, there's an unmet need for a novel class of anticancer agents specifically targeting BC cells [6]. Modern research has identified a plethora of potent bioactive compounds from both natural sources and synthetic methods that exhibit strong anticancer properties, suitable for BC chemotherapy [7]. This review highlights the recent discovery of newly synthesized anti-breast cancer compounds, contributing to our understanding of innovative synthetic compounds and paving the way for further exploration in the field.

Invasive breast cancer presents significant challenges due to its aggressive nature [8,9]. Enhancing long-term survival hinges on the ability to curb distant metastasis [10,11]. Effective breast cancer treatment relies on targeting specific mechanisms using existing natural or synthetic compounds with anti-tumor properties.12,13A review of the literature highlights the development of numerous heterocyclic and other molecular frameworks as potential anti-breast cancer agents [14-16].

Female breast cancer can be classified into four primary subtypes: [17]

• Luminal A: Tumours in this category are HER2 negative (HER2-), but they also express the oestrogen and/or progesterone receptors. They have low quantities of the protein Ki-67, which aids in regulating the proliferation of cancer cells. The prognosis for lumi-

nal A tumours is often good due to their low-grade characteristics and sluggish growth.

• Luminal B: Tumours in this category are PR-negative but positive for ER and HER2. They have a lot of the protein Ki-67. Breast cancers classified as luminal B have a marginally worse prognosis than luminal A tumours and frequently grow more quickly.

• HER2-enriched (HR-/HER2+) tumours: These tumours are HER2-positive but ER- and PR-negative. Targeted medicines that concentrate on the HER2 protein are used to treat them. HER2-enriched tumours have a worse prognosis than Luminal malignancies and grow more quickly. Pertuzumab, Trastuzumab Deruxtecan, Trastuzumab Emtansine, Lapatinib, Trastuzumab, and Neratinib are a few examples of targeted therapy.

• Basal-like: This subtype of breast cancer, also called triple-negative breast cancer, lacks the proteins ER, PR, and HER2. Most BRCA1 gene-mutated women experience it, especially younger African-American women. Breast cancer with basal-like characteristics is aggressive and lacks the three biomarkers (ER, PR, and HER2), making it a difficult form to treat.

2. Traditional Treatment: Consequences and Effects

The management of breast cancer involves various treatment approaches, including chemotherapy, radiotherapy, surgery, and hormonal therapy.18 Early-stage breast cancer (stages I and II) can often be effectively treated with radiotherapy and chemotherapy while preserving breast tissue [19].

However, managing breast cancer is complicated by the development of multidrug resistance, which can lead to fatal outcomes. Understanding the molecular basis of drug resistance and developing new drugs to target it is crucial [20,21].

Resistance to chemotherapy can occur through different mechanisms, with drug efflux membrane transporters like P-glycoprotein, MRP1, and BCRP playing a primary role [22,23]. This resistance can render previously effective drugs ineffective, such as anthracyclines, taxanes, and capecitabine. Additionally, using monotherapy in breast cancer treatment can promote the growth of new cancer cells within the tumor [24].

Furthermore, chemotherapy often leads to side effects such as a reduction in white blood cells and red blood cells, increasing the risk of infection and anemia [25,26]. Given these challenges, there is an urgent need to explore alternative approaches to breast cancer management that can minimize unexpected side effects associated with conventional treatments [27].

3. New Drugs Approved for the Treatment of Breast Cancer

The following sections provide a list of drugs that have been authorised by the FDA for use in treating different BC subtypes.

3.1. Everolimus

Everolimus is a medication derived from sirolimus and is an inhibitor of mTOR. It received FDA approval in July 2012 for the treatment of advanced HR+/HER2− breast cancer in post-menopausal women. It has also been approved for various other medical conditions, including tuberous sclerosis complex-associated partial-onset seizures in 2018, progressive, nonfunctional gastrointestinal and lung neuroendocrine tumors in 2016, and advanced pancreatic neuroendocrine tumors in 2011. Additionally, Everolimus is the first approved pediatric-specific dosage form for the management of a rare pediatric brain tumor called subependymal giant cell astrocytoma [28-30] (Figure 1).

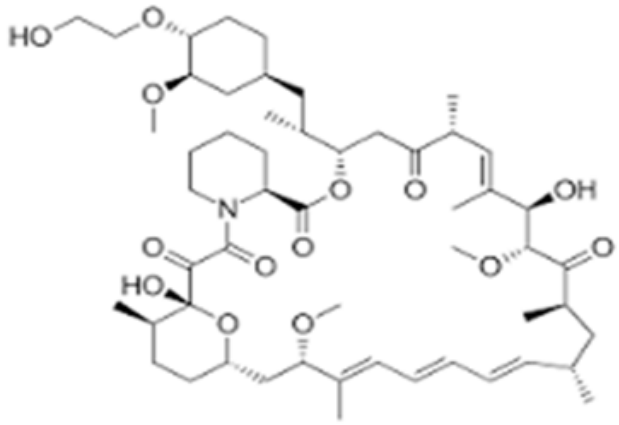

Figure 1:

3.2. Neratinib

Neratinib is an orally bioavailable kinase inhibitor that targets EGFR, HER2, and HER4. It acts as an irreversible pan-ErbB inhibitor by targeting the intracellular domain of these receptors, leading to reduced phosphorylation and downstream pathway activation. It has received recent FDA and EMA approval for the extended adjuvant treatment of early-stage HER2-positive breast cancer [31] (Figure 2).

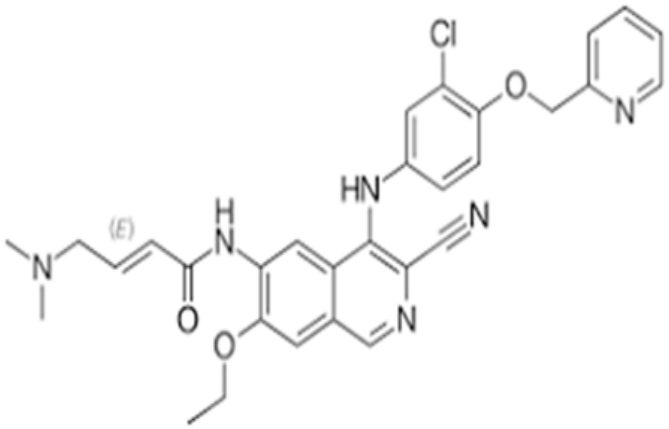

Figure 2:

3.3. Palbociclib

Palbociclib is a selective CDK4/6 inhibitor, belonging to the pyrido[2,3-d] pyrimidin-7-one derivative class. It received accelerated FDA approval on February 3, 2015, for use in combination with letrozole to treat advanced breast cancer in postmenopausal women. In 2016, it was further approved for the treatment of HR+/HER2− metastatic breast cancer. Palbociclib holds the distinction of being the first-in-class CDK 4/6 inhibitor to receive FDA approval [32] (Figure 3).

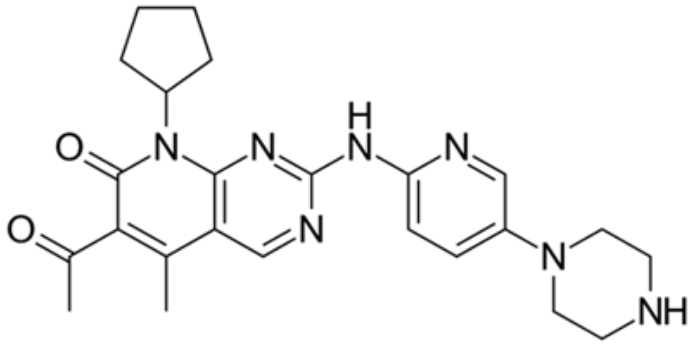

Figure 3:

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