



## Mini Review

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# Novel Approaches for Treatment of Breast Cancer Tumors



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## Abstract

In the last few years, various new drugs have been introduced on the international markets to treat breast cancer. These drugs are administered either orally or via an injection. In this article, we provide an insight into the current pipeline of drugs introduced during the last seven years. These drugs minimize toxicity and improve efficiency. They offer greater benefits to patients and have reduced side effects.

## Introduction

Breast cancer is the most commonly diagnosed cancer among females worldwide, with an estimated 14.1 million reported cases [1]. Cancer cells form a tumor when they have lost the ability to stop reproduction and enter the death phase at the proper time. A solid tumor comprises two parts:

- Tumor parenchyma.
- The stroma. The stroma contains the blood vessels and other supporting cells. As the tumor grows, the pre-existing blood vessels experience increased pressure which limits blood flow.

The idea of targeted killing of a cancer tumor originated in 1906 when Ehrlich introduced the concept of drug targeting of cancer cells by tissue-specific carriers that can deliver toxic agents to neoplastic tissue [2]. The advancements in nanotechnology have revolutionized drug delivery in oncology by introducing advanced therapeutic systems for cancer treatment [3]. There are currently three different signal transduction pathways that are targeted for the purposed of adjuvant breast cancer treatment by the use of hormone-blocking agents, chemotherapy and monoclonal antibodies.

### Targeting of EGFR (HER2)/neu signaling pathway

The human epidermal growth factor receptor (EGFR or HER2) is a tyrosine kinase receptor (Figure 1). These proteins serve as cell surface receptors in healthy cells and play important roles in signal transduction pathways [4]. Currently, Trastuzumab (Herceptin®) [5], a monoclonal antibody inhibitor and Lapatinib (Tyverb/Tykerb®) [6], a dual

EGFR/HER2 kinase inhibitor, are used for the treatment of HER2-positive cancers. Small molecule tyrosine kinase inhibitors have also provided attractive therapeutic agents, as they are able to block cell signaling associated with many of the proposed mechanisms for HER2 resistance.

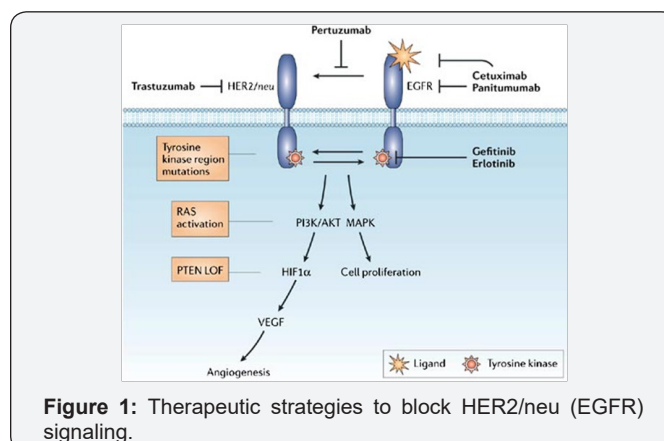
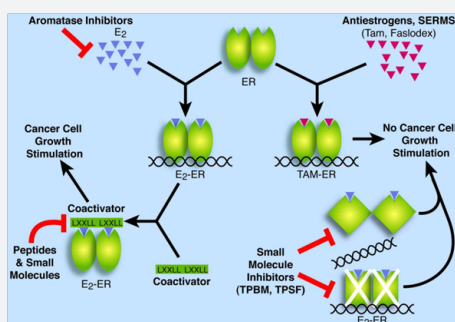


Figure 1: Therapeutic strategies to block HER2/neu (EGFR) signaling.

### Targeting of estrogen receptor (ER) signaling pathway

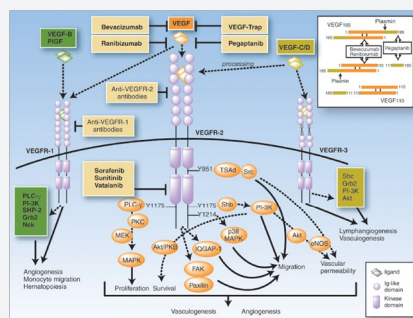
The majority of breast cancer tumors over-express the estrogen receptor (ER) $\alpha$  which regulates transcription and drives estrogen-stimulated proliferation of ER+ tumor cells (Figure 2) [7]. ER + patients usually receive adjuvant anti-estrogen therapy that relies upon on ER modification, down-regulation, or estrogen depletion [8]. Tumors often develop resistance to anti-estrogen therapy through stimulation of ER itself or of downstream mediators of ER-driven transcription, as well as activation of alternative proliferation pathways, in particular those driven by HER2/EGFR.



**Figure 2:** Schematic showing the different strategies that have been used to target the Estrogen receptor (ER) during therapy for breast cancer

## Targeting of vascular endothelial growth factor receptor-2 (VEGFR2) signaling pathway

Vascular endothelial growth factors (VEGF) and their receptors play an important role in blood vessel formation (Figure 3) [9,10]. Mice lacking various VEGF ligands or receptors show defects in vascular formation and maturation [3]. Members of the VEGF family are also involved in other biological processes, such as lymphangiogenesis, vascular permeability, and hematopoiesis. VEGF is released by tumor cells and induces tumor neo vascularization.



**Figure 3:** Schematic showing strategies for inhibition of tumor growth by anti-angiogenic therapeutic drugs.

## Conclusion

Over the past seven years, significant improvements have been made in breast cancer treatment. The development of the field of molecular biology has made the treatment of different types of breast cancers more efficient. Drugs are now being

designed to target molecules of signaling pathways that are important for cancer cell survival and proliferation. Estrogen receptor and HER2 signaling pathways have emerged as the most important targets for these drugs. Anti-HER2 targeted therapies have improved survival rates by 15%-23% in patients suffering from HER2 over-expressing breast cancers.

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