# A BRIEF REVIEW ON DRUG USED IN BREAST CANCER TREATMENT

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# ABSTRACT:-

With over 2 million new cases in 2020, breast cancer (BC) is the most common cancer diagnosed in women worldwide. Because of improved cancer detection, improved risk factor profiles, and improved cancer registration, its incidence and death rates have risen during the past three decades. Both modifiable and nonmodifiable risk factors are included in the substantial number of BC risk factors. Currently, people over 50 make up around 80% of BC patients. Both stage and molecular subtype affect survival. Wide spectrum tumors that vary in their shape, behavior, and clinical presentation are referred to as invasive BCs.Breast cancer treatment is complicated and includes a variety of approaches, such as hormone therapy, chemotherapy, radiotherapy, surgery, and biological therapies administered in various orders.

Keyword:- Epidemiology, risk factors, classification, diagnosis, prognosis, marker, and treatment of breast cancer

# INTRODUCTION :-

Breast cancer is a condition where tumors are formed when aberrant breast cells proliferate uncontrollably. These cells start in the breast's milk duct and milk-producing lobules. Both males and females can develop it.A particularly frequent form of cancer among women is breast cancer. Majority of it falls into two groups. A type of breast cancer known as ductal carcinoma originates in the lobules of the ducts. carcinoma of the lobules (1). This can also be further classified into different subtypes, the most common of which is ductal cancer. Breast cancer has the potential to spread to other body regions including lymph nodes (2). The majority of breast tumors begin as benign fibrocysts and turn malignant when they begin to Overexpression of hormone-specific or epidermal growth factor-specific receptors is a hallmark of breast cancer. Moreover, the stage and grade of breast cancer are taken into account when classifying the disease.There are many different medications and treatments that are either on the market or in the process of developing, given the volume of active research. Personalized therapy and chemotherapy rely on well-established medications, such as aromatase inhibitors (3). This article aims to review the available data on all FDA-approved medications for breast cancer, taking into account the drug's chemical makeup, class, dosage, clinical pharmacology,

treatments, mechanism of action, clinical efficacy, and ongoing research directions. Additionally, an attempt has been made to show and discuss each registered therapeutic molecule in the review paper. We think that this thorough analysis will serve as the go-to resource for information on any aspect of an anticancer medication that is now available on the market and has been given FDA approval for the treatment of breast cancer.(4) The glandular tissues of the breast produce and guarantee the passage of breast milk, while the lymphatic tissues, which are attached to the immune system and extract waste materials from cells, serve as supporting tissues. The stromal tissues are composed of fatty and fibrous connective tissues. Breast cancer can be categorized into various categories based on its locations and degree of invasiveness (5).

# SING AND SYMPTOMS :-

Breast cancer arises from the mutation of breast cells into malignant cells, which proliferate and eventually form tumors. Although it can sometimes afflict men and persons assigned male at birth (AMAB), as well as younger women, breast cancer usually affects women and individuals designated female at birth (AFAB) who are 50 years of age and older. Medical professionals may use chemotherapy to eradicate malignant cells or surgery to remove tumors in order to treat breast cancer (6).One of the earliest indications of breast cancer is frequently a lump or mass in the breastTrusted Source. These bumps are frequently painless. A person may feel as though their menstrual cycle is connected to pain in the breast or nipple area.Breast cancer usually causes gradual pain. Anyone experiencing breast pain ought to speak with a medical practitioner, particularly if it is severe or ongoing.A woman's breasts consist of thousands of lobules, connective tissue, and fat after puberty.These are tiny glands that can produce milk. These can be associated withTrusted Source exposure to estrogen, inherited genetic defects, or inherited genes that can cause cancer, such as the BRCA1 and BRCA2 genes (7).

OTHER POSSIBLE SYMPTOMS OF BREAST CANCER INCLUDE:-

-Swelling of all or part of a breast (even if no lump is felt

* Dimpling of the skin that occasionally resembles an orange peel
* Nipple or breast pain
* Nipple retraction, or inward rotation
* Breast or breast skin that is peeling, red, dry, or thickened
* Breast milk-like discharge from the breasts
* Enlarged lymph nodes in the vicinity of the collarbone or under the arm(In certain cases, this may indicate the spread of breast cancer before the initial tumor in the breast becomes noticeable.)
* Skin thickening, giving the appearance of orange peel
* Puckering or dimpling of the breast
* Nipple scaliness, perhaps extending to the areola
* Nipple alterations, such as inward twisting and pulling to one side (4)

BREAST CANCER DIAGNOSIS:-

# MAMMAGRAPHY-

An x-ray of the breast called a mammography might show abnormalities that are benign or cancerous. An x-ray image is created by passing a tiny amount of radiation through the breast after compression between two plates. Mammograms can be used for diagnosis as well as screening (8) .

Mammography screening is done in an effort to find any early indications of breast cancer—even before symptoms appear—in order to reduce mortality through prompt detection. If a woman has symptoms of breast cancer, such as a palpable lump in her breast, a diagnostic mammography helps identify the disease (9).

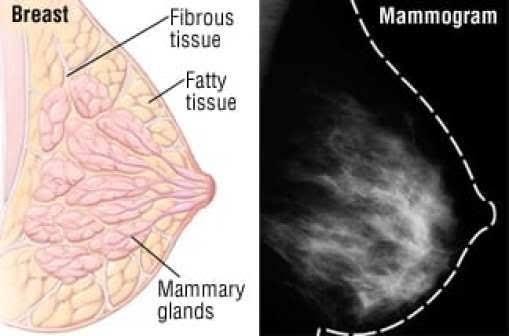


Fig - 1 Mammography

# MAGNETIC RESONANCE IMAGING-

Breast magnetic resonance imaging (MRI) is a non-invasive, non-ionizing diagnostic imaging technique that uses a magnetic field and low-energy radio frequency radiation to produce detailed images of the structures inside the breast. For women with a history of breast cancer, MRI can be used to assess the tumor's size and search for metastasized tumors. Using MRI, tumors less than or equal to 2 cm in size have been precisely detected and measured. However, because aberrant breast tissue surrounds the real lesion, larger breast tumors are frequently exaggerated, which can result in higher rates of mastectomy (8).

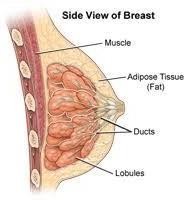


Fig - 2 Magnetic Resonance Imaging

# DYNAMIC CONTRAST IMAGING MRI (DCE - MRT)-

The method used in dynamic contrast-agent enhanced breast MRI is to examine the tissue's pattern of temporal enhancement after an intravenous infusion of a paramagnetic contrast agent. The degree of tissue vascularization, the make-up of interstitial spaces, and the

differentiation of lesions are all quantitatively assessed using this non-invasive imaging method (9).

# MAGNETIC RESONANCE ELASTOGRAPHY-

Tissue mechanical properties can be elucidated in vivo using magnetic resonance elastography (MRE). Breast MRE is a non-invasive, non-ionizing, cross-sectional imaging method that can quantify the viscoelastic characteristics of breast tissues after an external stress is applied. Because breast tumors contain more cells, collagen, and proteoglycans than benign lesions and normal surrounding tissues, they are frequently more rigid than benign lesions (10).

# MAGNETIC RESONANCE SPECTROSCOPY-

By applying strong magnetic field strengths (usually 11–14 T) to body fluids, cell extracts, and tissue samples, magnetic resonance spectroscopy (MRS) can quantify a chemical "spectrum" in the area and provide more details about the region's chemical composition (11).

FDA APPROVED IN BREAST CANCER:-

# PALBOCICLIB

The FDA awarded AA to the first CDK4/6i in 2015 so that it could be used in conjunction with letrozole as the first endocrine-based therapy for postmenopausal women who had HR- positive, HER2-negative advanced or MBC. Although the PALOMA-1 trial showed a significant improvement in median PFS, an AA was awarded because to the trial's limited size and its unreliability. The use of any aromatase inhibitor (AI) in conjunction with this indication was broadened in 2017 and elevated to regular approval (RA) due to consistent outcomes from a larger randomized PALOMA-2 trial conducted in the same environment (12).

# RIBOCICLIB

For the treatment of postmenopausal women, ribociclib plus an AI was approved in 2017 based on the results of the randomized, double-blind, placebo-controlled MONALEESA-2 trial. In 2018, the indication was broadened for premenopausal women in conjunction with an AI, based on the outcomes of the randomized, double-blind, placebo-controlled MONALEESA-7 trial. Based on data from a randomized double-blind, placebo-controlled trial that showed a significant median PFS, ribociclib was also approved in combination with fulvestrant for postmenopausal women with HR-positive, HER2-negative advanced or MBC, either as initial endocrine-based therapy or after disease progression on endocrine therapy. Letrozole and ribociclib were approved as a co-package in 2017(13).

# ABEMACICLIB

Based on MONARCH-2, a placebo-controlled, randomized trial, abemaciclib plus fulvestrant received RA in 2017 for women with HRpositive, HER2-negative advanced or MBC. Furthermore, in the metastatic context, abemaciclib was authorized as a monotherapy for both males and females with HR-positive, HER2-negative advanced or MBC whose illness progressed after prior chemotherapy and endocrine therapy. Based on MONARCH-1, a single-arm experiment that showed a significant objective response rate (ORR) and median duration of response (DoR), the approval as monotherapy. Based on the results of the randomized, double- blind, placebo-controlled MONARCH-3 trial, which showed a significant improvement in abemaciclib's median PFS when compared to placebo, abemaciclib was given RA in 2018 along with an AI for the treatment of postmenopausal women with HRpositive, HER2-negative advanced or MBC (14).

# ELACESTIRANT

Elacetrant (Orserdu, Stemline Therapeutics, Inc.) was approved by the Food and Drug Administration (FDA) on January 27, 2023, for use in postmenopausal women or adult men who have advanced or metastatic breast cancer that is ER-positive, HER2-negative, and has an ESR1 mutation. The disease progression must have occurred after at least one line of endocrine therapy (15).

# LAPATINIB

2010 saw the AA approval of this oral tyrosine kinase inhibitor of HER2 (first approved in 2007) for use in conjunction with letrozole in the treatment of postmenopausal women with HR-positive MBC (mouse-behaving cancer) that overexpresses the HER2 receptor and is recommended for hormonal therapy. A double-blind, placebo-controlled trial that showed a considerable median PFS improvement in the HER2-positive population served as the basis for approval. Among the trial's HER2-negative population, no benefits were observed. In 2018, this indication was changed to RA due to a statistically significant and clinically relevant improvement in PFS seen in the EGF114299/LAP016A2307 study (16).

# TALAZOPARI

2018 saw the approval of talazoparib, a PARP inhibitor, for use in patients with HER2- negative locally advanced cancer (MBC), deleterious or suspected detrimental gBRCAm, or both. The approval was based on EMBRACA, an open-label trial that randomly assigned patients with gBRCAm HER2-negative locally advanced or metastatic breast cancer to receive either

talazoparib or the chemotherapy of their choice from their oncologist. When talazoparib was used instead of chemotherapy, the median PFS was significantly higher (17).

# T\_Dxd

For the treatment of patients with unresectable or metastatic HER2-positive BC who have had two or more prior antiHER2-based regimens in the metastatic context, T-DXd, an ADC targeting HER2, was awarded AA in 2019. Treatment options were restricted for HER2-positive patients at the time of AA after two lines of therapy, and the results showed considerable benefits above currently available medications for a population heavily pretreated (18).

# NERATINIB

In 2020, patients with HER2-positive advanced or MBC who had received two or more previous antiHER2 based regimens in the metastatic situation were given RA in addition to capecitabine, an oral TKI that targets HER2. The NALA open-label trial, which randomized patients with HER2-positive MBC to either lapatinib and capecitabine or neratinib and capecitabine, served as the basis for the approval. There was a discernible improvement in the median PFS. The 12- and 24-month PFS analyses and Hazard Ratio preferred the neratinib arm, despite the fact that the median PFS data was equal between the arms. Neratinib, which was previously limited to use in the early stages of breast cancer treatment, is now an additional option for patients who have received extensive pretreatment when their cancer has spread (19).

# OLAPARIB

The first PARP drug approved by RA for use in treating patients with HER2-negative MBC and deleterious or presumed detrimental gBRCAm who have had chemotherapy in a neoadjuvant, adjuvant, or metastatic setting was olaparib in 2018 (20).

# ALPELISIB

In 2019, RA was administered in conjunction with full vstrant for patients diagnosed with HR-positive, HER2-negative, PIK3CA-mutated, advanced, or MBC cancers as determined by an FDA-approved test after progression on or after an endocrine-based therapy. Alpelisib is an oral alpha-specific PI3K inhibitor. Based on a randomized, double-blind, placebo-controlled trial, SOLAR-1 was the first PI3K inhibitor approved by the FDA for the treatment of breast cancer. In the group of patients with PIK3CA tumor mutations, the median PFS was substantial.Of note, only 6% of study participants had received an AI + CDK inhibitor and Nonetheless, despite the modest size of this sample and its broad confidence intervals, the PFS data supported the use of alepelisib (21).

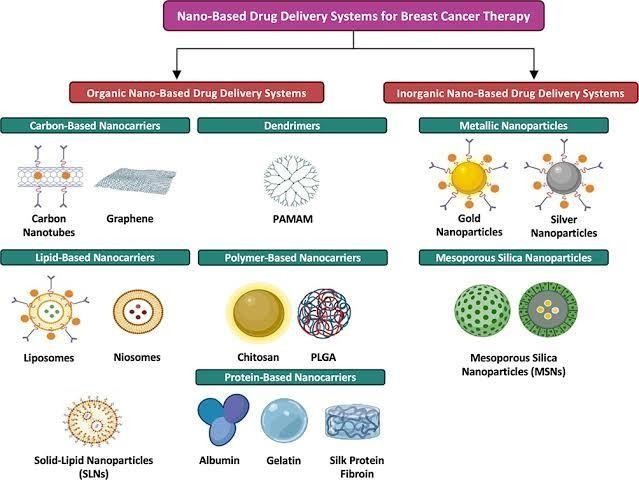
# TUCATINIB

For adult patients with advanced unresectable or metastatic HER2-positive BC, including those with brain metastases, who have received one or more previous anti-HER2-based regimens in the metastatic setting, tucatinib, an HER2CLIMB, a randomized, double-blind, placebo-controlled trial that included patients with HER2-positive MBC who had previously had treatment with trastuzumab, pertuzumab, and T-DM1, demonstrated efficacy. When compared to the control group of capecitabine and trastuzumab, the median PFS and OS for tucatinib, trastuzumab, and capecitabine were significant. When comparing the median progression-free survival (PFS) between the tucatinib and control groups of patients with baseline brain metastases, there was a significant difference. This approval was the first to assess a new molecular entity under OCE's Project Orbis, and it was the first to include the treatment of brain metastases in the indication (22).

# BREAST CANCER AND TREATMENT METHODOLOGIES:-

Depending on the kind of cell involved, breast cancer can be categorized as either connective tissue BC, lobular BC, or ductal BC. Certain cancer cells exhibit overexpression of select hormone receptors, such as those for estrogen, progesterone, or the HER-2 gene (Orrantia-Borunda et al., 2022). On the other hand, other cancer cells may exhibit mutations in the p53 gene and other molecular markers, such as let-7, miR-155, miR-150, and miR-153. This knowledge help clinicians to build more personalized, focused and effective therapy for the patient (Curigliano and Criscitiello, 2014; Nounou et al., 2015).The menopausal state affects the pharmaceutical selection. There are three stages of treatment for nonmetastatic breast cancer. Systemic endocrine or immunotherapies (ER, PR, or ERBB2 positive patients) are used during the preoperative phase. The only treatment available when tumors lack any of the three receptors is preoperative chemotherapy.The oral distribution of cancer chemotherapeutic drugs has always been difficult because of first-pass metabolism, gastrointestinal adverse effects, and limited bioavailability. Anticancer medications are available in a broad range of dose forms, drug carriers, and drug delivery systems. These options include both innovative drug delivery methods and the traditional mode of treatment, which are emerging as viable alternatives for the management of breast cancer.There are several typical dose forms on the market for oral administration, such as tablets, capsules, and suspensions.The vast amount of data available indicates that, despite the fact that the majority of nanomedicines are still in the research or clinical trial stages and have not yet made it to market, the field's extensive research will undoubtedly result in a revolutionary shift in treatment approaches in the near future (23).

# Breast cancer and treatment methodologies :-



**Fig - 3 Pectorial representationo of convention and novel formulation of various FDA approved anti cancer drug used for breast cancer indication.**

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