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Review

Breast Cancer Post Market Monitoring of Drugs & Procurement Strategies

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Abstract

Breast cancer represents a formidable global health challenge, necessitating continual advancements in treatment modalities and healthcare delivery. This research paper explores the pivotal intersection of post-market monitoring of breast cancer drugs and strategic procurement strategies, aiming to optimize patient outcomes while ensuring accessibility and affordability. Beginning with an overview of the current landscape, this paper investigates the methodologies and regulatory frameworks governing post-market monitoring breast cancer drugs. It scrutinizes the strengths and limitations of existing surveillance mechanisms, including spontaneous reporting systems and real-world evidence generation, and examines emerging trends such as Pharmacovigilance in digital health platforms. This paper delves into the complexities of drug procurement, analyzing various strategies employed by healthcare systems and stakeholders to enhance accessibility and affordability.

Keywords: *Breast Cancer, Raloxifene, Tamoxifen, Bioavailability, Treatment, Toxic, Breast, Patient, Mechanism.*

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1.Introduction

Breast cancer a disease in which cells in the breast grow out of control. There are different kind of breast cancer. The kind of breast cancer depends on which cells in the breast turn into cancer. Mainly breast cancer begins in the ducts or lobules it can spread outside the breast through bloods vessels and lymph vessels. When breast cancer spreads to others parts of the body, it is had metastasized. Men and women are both affected but women experience it more frequently.

What is breast cancer

Most frequently from the lobules that supply the milk ducts with milk or the inner lining of the milk ducts. Cancers that start in the ducts are called ductal carcinomas, and cancers that start in the lobules are called lobular carcinomas.

Types of Breast Cancer

There are many types of breast cancer

1. Ductal carcinoma in citu (DCIS)
2. Invasive Ductal Carcinoma
3. Inflammatory Breast Cancer
4. Metastatic Breast Cancer
5. Some other specific types.

2. Etiology

When you're told that someone have breast cancer, it's natural to wonder what may have caused the disease.

- But no one knows the exact causesof breast cancer.

- Doctors seldom know why one woman develops breast cancer and another doesn't, and most women who have breast cancer will never be
- able to pinpoint an exact cause. What we do know is that breast cancer is always caused by damage to a cell's DNA.

In few years estimated

In 2018, breast cancer emerged as the most prevalent cancer among women in India, constituting 27.7% of all newly diagnosed cases. Shockingly, a woman was diagnosed with breast cancer every four minutes, while the disease claimed a life every eight minutes. The figures for that year revealed 162,468 new case and 87,090 deaths, making India the second-highest contributor to breast cancer mortality globally in 2018.[6][8]

Breast cancer Incidence

The number of women with breast cancer who were recently diagnosed is known as the incidence. In India, 162,468 women had a new diagnosis of breast cancer in 2018. Additionally, 27.7% of all newly discovered malignancies in women were breast cancers.[2]

Breast cancer Mortality

The quantity of ladies who passed away from breast cancer is known as mortality. In India, breast cancer claimed the lives of 87,090 women in 2018. In India, breast cancer was responsible for around 23.5% of all cancer-related fatalities among women[4]. This indicates that breast cancer accounted for nearly one in four cancer-related fatalities among Indian women.

S.No	Indication	Indication	Dosage	Mechanism of action	Efficacy	Adverse Effects	Interaction
1.	Raloxifene	FDA approved for postmeno-pausal women with osteoporosis and at high risk for breast cancer (should not used in premenopausal women)	60 mg orally daity for 5 years	Benzothiophene derivative: an anti-estrogen similar to tamoxifen but a full antagonist at uterine tissue, resulting in lower endometrial cancer risk	Decreased risk of Invasive breast cancer 76%	Has lower risk of uterine cancer and blood clot in the legs or lungs compared to tamoxilen: increasing risk of DVT or PE and risk of death due the stroke increase in women with coronary events	Bile acid sequestrants and levothyroxine decrease absorption of raloxifene Risk D: consider therapy modification). Raloxifene increases adverse toxic effect of osperitene (Risk X* avoid concurrent use)
2.	Tamoxifen	Prevention of Invasive breast cancer in women at high risk, ER+ (atypical hyperplasia or LCIS and postmenopausal women with a family history)	20 mg orally daily for 5 year	An antiestrogen: binds and blocks estrogen receptors and thus blocks estrogen from acting on cells are not cancerous.	Breast cancer reduction : 45%-49%	Black box warning: increased incidence of uterine or endometrial malignancies (some fatal) for Perimenopausal women with intact uterus: serious blood clots, stroke, and PE (rare)	SSRis: strong CYP206 Inhibitors (fluoxetine, paroxetine) and moderate CYP2D6 inhibitor (sertraline) decrease tamoxifen efficacy, concurrent use with paroxetine Increases Probability of death breast cance

3. Drugs approved to prevent breast cancer

a) Raloxifene Hydrochloride
b) Tamoxifen Citrate

4. Drugs Approved to Treat Breast cancer

a) Abemaciclib
b) Abraxane (Paclitaxel Albumin-stabilized
c) Nanoparticle Formulation)
d) Ado-Trastuzumab Emtansine
e) Afinitor (Everolimus)
f) Afinitor Disperz (Everolimus)
g) Alpelisib
h) Anastrozole
i) Aredia (Pamidronate Disodium)
j) Arimidex (Anastrozole)
k) Aromasin (Exemestane)
l) Capecitabine
m) Capivasertib
n) Cyclophosphamide
o) Docetaxel
p) Doxorubicin Hydrochloride
q) Elacestrant Dihydrochloride
r) Ellence (Epirubicin Hydrochloride)

s) Enhertu (Fam-Trastuzumab Deruxtecan-nxki)
t) Epirubicin Hydrochloride
u) Eribulin Mesylate
v) Everolimus
w) Exemestane

Drugs	Patients	Cure rate
Raloxifene Hydrochloride	22	1.6%
Tamoxifen Citrate	58	1.3%

Raloxifene: Raloxifene is medication primarily prescribed for postmenopausal women. It serves two main purposes: treating osteoporosis, a condition characterized by weakened bones and increased fracture risk, and reducing the chance of postmenopausal women developing invasive breast cancer. Raloxifene is an estrogen receptor that is selective modulator, meaning it interacts with estrogen receptors in a specific way[8]. It acts as an agonist (activator) on bone receptors, mimicking some effects of estrogen, which helps improve bone density and strength. However, it acts as an antagonist (blocker) on other estrogen receptors, which helps lower the chance of breast cancer. Overall, Raloxifene offers a dual benefit by addressing both osteoporosis and risk of breast cancer in postmenopausal women.[9]

Mechanism of Action: Raloxifene acts by binding to estrogen receptors, eliciting both estrogenic and anti-estrogenic effects depending on the tissue. Its mechanism involves binding to two isoforms of estrogen receptors: alpha (which activates) and beta (which inhibits). This modulation of receptor expression alters cellular and tissue responses to estrogen. Raloxifene has a low bioavailability of around 2%, attributed to its absorption rate of 60%. Itsonset of action is observed after eight weeks. The drug is predominantly bound to proteins (>95%) during distribution. Metabolism primarily takes place in the liver, and excretion predominantly occurs via feces (>93%) with minimal urinary excretion (<0.2%).

Adverse reaction: The most commonly reported adverse effects of raloxifene include hot flashes, flu-like symptoms, muscle spasms, arthralgia, and infections. Less frequent side effects encompass insomnia, vomiting, sinusitis, deep venous thrombosis (DVT), bronchitis, pharyngitis, and breast pain. In women receiving raloxifene treatment, the reported adverse effects included peripheral edema (raloxifene 14.1% vs placebo 11.7%), muscle spasms/leg cramps (12.1% vs 8.3%), hot flashes (7.8% vs 4.7%), cholelithiasis (3.3% vs 2.6%), and venous thromboembolic events (2.0% vs 1.4%). The most serious adverse reactions related to raloxifene is venous thromboembolism (pulmonary embolism, deep venous thrombosis, and retinal vein thrombosis)

Monitoring: Patients taking raloxifene should monitored for symptoms suggestive of deep vein thrombosis (DVT), such as calf or lower limb redness, tenderness, and inflammation. Immediate evaluation at the emergency department is advised if such symptoms arise, with a Doppler ultrasound of the lower limbs to confirm or rule out DVT. Positive findings may necessitate hospital admission. For patients expected to be immobilized, raloxifene should be suspended 72 hrs. prior and during this period. Close monitoring of prothrombin time is recommended when raloxifene is co-administered with warfarin and its derivatives.[12] Supplementation with vitamin D and calcium is advised alongside raloxifene therapy. Additionally, regular monitoring of hepatic profile and triglyceride levels is recommended due to estrogen's effect triglycerides.

Tamoxifen: Tamoxifen is a hormone therapy used to treated hormone receptor-positive breast cancer. It can greatly lower the risk of cancer recurrence (return) and invasive cancer. Some people take tamoxifen to reduce the risk of developing breast cancer

Mechanism of Action: Tamoxifen selective estrogen receptor modulator (SERM), displays both estrogenic and antiestrogenic effects based on its binding location. In breast tissue, it competes with estrogen, acting as an antagonist, thereby exhibiting antiestrogenic and antitumor properties by slowing cell cycling. This makes it cytostatic. Conversely, in bone, it acts as an estrogen agonist, stimulating estrogen receptors and potentially preventing osteoporosis in postmenopausal women. These dual actions make tamoxifen a patient-specific treatment for [BD] Breast cancer. In premenopausal women, tamoxifen acts as estrogen agonist in the hypothalamus, leading to increased gonadotropin levels and potentially inducing ovulation. However, its mechanism of actions in McCune-Albright syndrome is still unclear.

Adverse Effects: Tamoxifen carries a black box warning due to its association with uterine malignancies, pulmonary embolisms, or stroke, particularly in high-risk cancer patients or those with Ductal carcinoma in situ. In females, it used linked to an elevated risk of uterine or endometrial cancers, some of which may be fatal.[11] Despite these risks, patients already diagnosed with breast cancer, the benefits of tamoxifen generally outweigh the potential hazards.Tamoxifen, like numerous cancer medications, is linked to various adverse effects, though severe and fatal occurrences are uncommon. Mainly side effects during treatment encompass hot flashes, irregular periods, and vaginal discharge. Additionally, patients may experience peripheral edema, hypertension, mood changes, pain, depression, skin alterations, nausea, vomiting.

Toxicity: Approximately 5% of women discontinue tamoxifen due to side effects, primarily stemming from estrogen blockade. Common effects include hot flashes, vaginal discharge, menstrual irregularities, and fluid retention. Occasional symptoms comprise depression, headache, fatigue, and decreased concentration. Although thromboembolic events such as thrombophlebitis, pulmonary embolism, and deep venous thrombosis occur more frequently among tamoxifen users, the overall incidence remains low at 1% to 3%. Additionally, there's an increased risk of endometrial carcinoma associated with tamoxifen, particularly with longer durations and higher doses. However, predicting the exact risk in healthy women is challenging due to uncontrolled factors like breast cancer, hypertension, obesity, diabetes, and geographic location.[17]

Ocular effects such as macular degen-eration, retinopathy, and cataract formation have been reported, but have not been conclusively linked to the use of tamox-ifen. 24 However, an ophthalmologic evaluation is recommended if ocular problems arise.

Hepatic carcinoma has shown to increase in incidence with tamoxifen use in rats, but this association does not appear to exist in humans.

Result: The results of the research on Breast Cancer Post Market Monitoring of Drugs provide valuable insights into the safety, efficacy, and real-world impact of medications used in the treatment of breast cancer. Through systematic monitoring of post-market data, the study identifies potential adverse events, drug interactions, and long-term effects associated with breast cancer drugs. Identification of rare or unexpected adverse events: Post-market monitoring helps identify adverse events that may not have been evident during clinical trials due to their rarity or specific patient populations.

1. Assessment of treatment effectiveness: By analyzing real-world data, researchers can evaluate the effectiveness of breast cancer drugs in diverse patient populations and clinical settings, providing insights beyond the controlled environment of clinical trials.
2. Monitoring of drug utilization patterns: Post-market surveillance enables tracking of drug utilization patterns, including prescribing trends, adherence rates, and off-label use, informing healthcare decision-making and resource allocation.
3. Evaluation of long-term safety and efficacy: Longitudinal data analysis allows for the assessment of the long-term safety and efficacy of breast cancer drugs, including potential risks of cumulative toxicity and the emergence of late-onset adverse events.
4. Identification of factors influencing treatment outcomes: Post-market monitoring may reveal factors such as patient demographics, comorbidities, and concomitant medications that impact treatment outcomes, guiding personalized treatment approaches.

Conclusion: Breast Cancer Post Market Monitoring of Drugs & Procurement Strategies highlights the critical importance of vigilant surveillance and strategic procurement in the management of breast cancer.

- 1 out of every 100 women is treated successfully
- Chances of treatment are very low
- Risky foe women above 45yrs.
- Some drugs more side effect on patients
- Women are more likely from breast cancer

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