

Secondary Research on Treatment of Breast Cancer drugs: launched and marketed by Bio-pharmaceutical companies.

[At Prescient Health Group]

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MBA HM 2020-22

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Presentation Outline

Introduction

Objective

Methodology

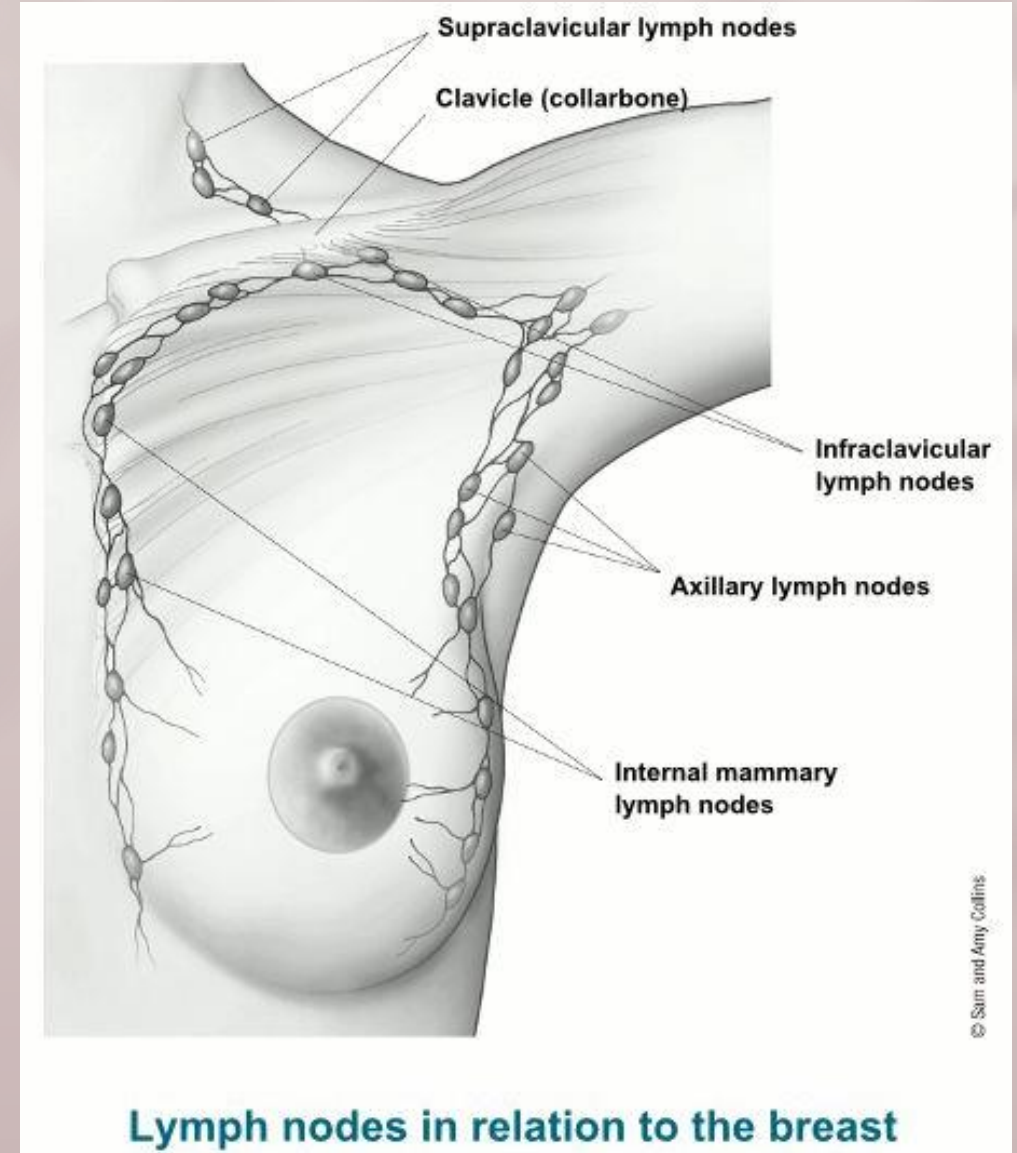
List of bio pharmaceutical companies and their drugs

Result

Conclusion

Breast Cancer

- Breast cancer is the number one cancer among Indian women.
- Breast cancer can spread when the cancer cells get into the blood or lymph system and are carried to other parts of the body.
- Most of the lymph vessels of the breast drain into:
 1. Lymph nodes under the arm (axillary nodes).
 2. Lymph nodes around the collar bone (supraclavicular [above the collar bone] and infraclavicular [below the collar bone].
 3. Lymph nodes inside the chest near the breastbone (internal mammary lymph nodes).
- If cancer cells have spread to your lymph nodes, there is a higher chance that the cells could have traveled through the lymph system and spread (metastasized) to other parts of your body.



How we classify breast cancer?

1. Breast cancer classification – Hormone Receptors

- The hormones steroid, oestrogen, and progesterone, which behave as "master regulators" of breast growth, have a substantial impact on puberty changes. By attaching to cellular receptors, the two steroid hormones work together to stimulate growth.
- The oestrogen receptors (ER) and/or progesterone receptors (PR) Hormones' role in carcinoma has long been known and drugs function by inhibiting cancer cells from utilising oestrogen or progesterone in several approaches.
- Oestrogen receptors comparatively more common than progesterone receptors, accounting for over 80% of all occurrences of hormone-dependent and oestrogen receptor-positive (ER+) breast cancer. Because oestrogen receptor-negative/progesterone receptor-positive (ER-/PR+) cancers are so rare, medications that target oestrogen-related pathways are often overlooked.
- The ER signaling cascade is disturbed when the oestrogen receptor is destroyed, robbing cancer cells of their ability to use oestrogen.
- It is often used to treat SERDs when a tumour has grown to different areas of the body, and it is gradually utilised in combination with alternative treatments to surmount endocrine endurance. The option available drugs for HR+ breast cancer has expanded dramatically in recent years. However, improvement scope is there. Attempting to profoundly alter the life expectancy of girls with HR+ illness.

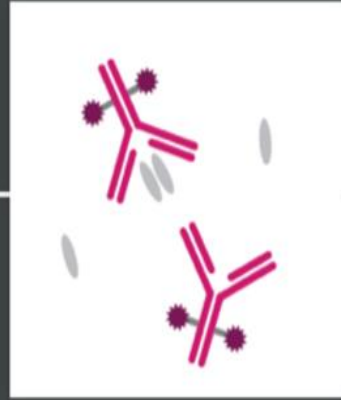
2. Breast cancer classification – HER2 receptors

- Human epidermal protein 2 (HER2) gene, which aids cell health.
- When the HER2 gene or protein is overexpressed in carcinoma cells, it promotes excessive neoplastic cell growth and proliferation.
- High levels of HER2 protein expression have been linked to severe diseases, a high rate of recurrence, and an increased risk of mortality in roughly 20% of breast cancers.
- Although HER2+ carcinoma has traditionally been linked with a poor prognosis, this has changed dramatically with the discovery of monoclonal anti-HER2 antibodies, tyrosine kinase inhibitors, and antibody-drug conjugates (ADCs) that target the oncogenic driver.
- ADCs are made up of two cancer-battling drugs: one with a cytotoxic component known as the chemical treatment or payload, and the other with a linker that joins an antibody and a cytotoxic substance (this links to a chosen cancer cell target). This enables for the extremely precise delivery of a known lethal agent with poor cancer cell selectivity into the somatic cell, which might potentially ignite regular cells.

How do ADCs work?



A cancer-killing drug is attached to the mAb through a stable connection (linker), creating the ADC



The ADC binds to specific proteins on the surface of cancer cells, and is then internalised into the cell



Once inside the cancer cell, the cytotoxic drug is released, destroying the cancer cell

ADC: Antibody-Drug Conjugate mAB: monoclonal Antibody

- ADCs comprises two cancer-fighting medications, one with a cytotoxic substance called chemical treatment or payload, and one with a linker combining an antibody (this links to a chosen cancer cell target).
- This allows for the very precise administration into the somatic cell of a recognised cytotoxic chemical with weak cancer cell selectivity that might possibly spark ordinary cell

3. Breast Cancer That Is Triple-negative Is Known As Triple Negative Breast Carcinoma (TNBC)

- Triple-negative breast cancers (TNBC) lack oestrogen receptors, progesterone receptors, and significant levels of HER2 overexpression, therefore they are classified as 'negative' for all three.
- This type of carcinoma is considered to be especially aggressive and rapid growing, with a high risk of metastasis, and, regrettably, it is more likely to return after therapy than other types of breast cancer.
- TNBCs are classified as "negative" for all three because they lack oestrogen receptors, progesterone receptors, and significant levels of HER2 overexpression. TNBC is more frequent in women under 40, accounting for 10-15% of all breast cancer cases. This type of carcinoma is recognized as highly volatile and rapid-increasing, with a high-level threat of metastasis, and it is, sadly, more expected than other types of breast cancer to relapse following treatment.
- The role of TNBC in directing therapy alternatives: The quantity of therapy alternatives accessible for TNBC is considerably lesser than for other forms of carcinoma due to a lack of established actionable biomarker targets. like the majority of breast cancer patients

Objective:

To know about different drugs that are launched and marketed by Bio-pharmaceutical companies for the treatment of Breast Cancer.

Methodology:

- It is a review-based study.
- Variety of drugs manufactured by bio-pharmaceutical companies for the treatment of breast cancer: variety of articles, research paper, conferences, available public domain data from organization websites and relevant sources document of last five years was thoroughly reviewed.
- **Keywords:** Breast cancer, Metastatic, HR+/HER2, Triple - Negative Carcinoma (TNBC), Hormone receptor.

Bio Pharmaceutical Companies And Ongoing Research on Cancer Drugs at PHG:

Company Name	Project	Product
Novartis	Breast cancer	Ribociclib (Kisqali), Alpelisib (Piqray)
Eli Lilly & Co.	Breast Cancer	Abemaciclib (Verzenio), LY3484356
Merus	Breast Cancer	Zenocutuzumab (MCLA-128)
Roche	Breast Cancer	Trastuzumab (Kadcycla), Pertuzumab (Perjeta), trastruzumab/pertuzumab FDC (Phesgo
G1 Therapeutics	Breast Cancer	Rintodestrant [BC]
MacroGenics	Breast Cancer	Margetuximab (Margenza) [BC]
Pfizer	Breast Cancer	Palbociclib (Ibrance) [BC]
AstraZeneca	Breast Cancer	Trastuzumab deruxtecan (Enhertu) [BC]
Gilead	Breast Cancer	Sacituzumab govitecan-hziy (Trodelvy) [BC]

Bio-pharmaceutical Companies & drugs:

- 1) ELI LILLY & Co. [Abemaciclib (Verzenio)]
- 2) Roche [Kadcyla (trastuzumab emtansine)]
- 3) AstraZenca [Trastuzumab deruxtecan (Enhertu)]
- 4) Gilead Sciences [Trodelvy (Sacituzumab)]

1) ELI LILLY & Co.

Drug: Abemaciclib (Verzenio)

Verzenio also mentioned as abemaciclib.

It is a drug which is taken:

- **Carcinoma called HR+/HER2–** (hormone receptor positive/human epidermal protein receptor 2–negative) and thus the cancer has spread to other parts of the body (metastasized).
- Verzenio is used as an initial endocrine-based therapy in conjunction with an inhibitor of aromatases for treating postmenopausal women in conjunction with fulvestrant in women whose disease has advanced after hormone therapy or in other cases in adults who progress from hormone therapy to previous chemotherapy.

The most common side effects of Verzonin include:

- Nausea
- Abdominal pain
- Infections
- Tiredness
- Low red cells counts (Anemia)
- Low white blood cells (Leukopenia)
- Decreased appetite
- Vomiting
- Headache
- Less platelet count (Thrombocytopenia)
- Hair thinning or hair loss (alopecia)

These aren't all the possible side effects of Verzonin

2) ROCHE

Roche is a main thing in the research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world's biggest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, and neuroscience.

Drug: Kadcyla (trastuzumab emtansine)

- It is an effective antibody-drug made to deliver potent chemotherapy on **to HER2-cancer cells**, limiting damage to healthy tissues. Two anti-cancer properties joined together by a stable linker in it and the HER2-targeting properties of trastuzumab and therefore chemotherapy agent DM1.
- Kadcyla is approved as a single agent in over 100 countries, including the US and EU, for the treatment of people with HER2-positive advanced breast cancer who have previously received Herceptin and taxane-based chemotherapy, either separately or together.
- Kadcyla is additionally approved within the US and EU for the adjuvant (post-surgery) treatment of individuals with HER2-positive early carcinoma with residual invasive disease after neoadjuvant (pre-surgery) treatment that included Herceptin and taxane-based chemotherapy.



Pertuzumab and trastuzumab:

- The HER2-targeted antibody trastuzumab was introduced in clinical and revolutionized the treatment of HER2-positive carcinoma patients. Despite this achievement, most patients with HER2-positive metastatic carcinoma still show progression of their disease, highlighting the necessity for brand spanking new therapies.
- The continuous interest in novel targeted agents led to the event of Pertuzumab, the primary during a new class of agents, the HER dimerization inhibitors. Pertuzumab may be a novel recombinant humanized antibody directed against extracellular domain II of HER2 protein that's required for the heterodimerization of HER2 with other HER receptors, resulting in the activation of downstream signalling pathways. Pertuzumab combined with trastuzumab plus docetaxel was approved for the first-line treatment of patients with HER2-positive metastatic carcinoma and is currently used as a typical of care during this indication.

3) AstraZenca

Drug: Trastuzumab deruxtecan (Enhertu)

Enhertu for **the treatment of adult patients with unresectable or metastatic HER2 negative/positive carcinoma** who have received two or more prior anti-HER2 based regimens within the metastatic setting.

HER2:

HER2 may be a tyrosine kinase receptor growth-promoting protein found on the surface of some cancer cells that's related to aggressive disease and poor prognosis in patients with carcinoma . To be considered HER2-positive, tumour cancer cells are usually tested by one among two methods: immunohistochemistry (IHC) or fluorescent in place hybridisation (FISH). IHC test results are categorized according to: 0, IHC 1+, IHC 2+, or IHC 3+. A finding of IHC 3+ and/or FISH amplification is taken into account positive.

- Enhertu may be a HER2-directed antibody-drug conjugate (ADC) and therefore the FDA approval is predicated on the results of the registrational phase II clinical trial DESTINY-Breast01 of Enhertu (5.4mg/kg) monotherapy in patients with HER2-positive metastatic breast cancer.
- Phase 2 clinical trial results told a confirmed objective response rate of 60.3% including a 4.3% complete response rate and a 56.0% partial response rate.
- The safety of Enhertu was assessed in a pooled analysis of data from both the phase II clinical trial DESTINY-Breast01 and the previous phase I clinical trial study among a total of 234 patients with metastatic HER2-positive cancer who received at least one dosage of Enhertu, 5.4mg/kg.
- The most common adverse reactions (greater than or adequate to 20% of patients) were nausea, fatigue, vomiting, alopecia, and constipation.
- Pneumonitis occurred in 9% of patients. Fatal outcomes to pneumonitis occurred in six patients i.e. 2.6% - 2 deaths previously reported within the phase I clinical trial and 4 deaths previously reported within the phase II clinical trial DESTINY-Breast01.
- Patients with the disease should be actively screened and monitored for potential signs and symptoms. If pneumonitis is diagnosed, it should be managed with dose modification and steroid treatment.

4) Gilead Sciences

Gilead Sciences, Inc. is a company that has received breakthroughs in medicine for quite three decades, with the goal of making a world healthy for all world. The company is dedicated in advancing medicines to stop and to treat diseases, including HIV, hepatitis , and cancer. Gilead operates in 35 countries worldwide.

Drug: Trodelvy

GileadSciences,Inc. has announced the complete approval of the U.S. Food & Drug Administration for Trodelvy by adult patients receiving two or more prior systemic treatments for metastatic illness with **locally advanced or metastatic triple negativity carcinoma (TNAC)**. The approval is supported by Phase Three ASCENT data in which Trodelvy has shown a 57% reduction in the probability of a disease deepening or death that is statistically significant and clinically significant.

The Indication of Trodelvy involves therapy of patients who have received two or more previous systemic treatments with unresectable, locally progressed or metastatic TNBC, including at minimum one for metastatic illness.

Trodelvy is being manufactured as an investigational treatment for metastatic urothelial cancer, hormone receptor-positive/2-negative, metastatic breast cancer and metastatic non-small cell lung cancer.

ASCENT Study:

The Phase three ASCENT study, an open-label, randomized confirmatory trial, enrolled quite 500 patients with relapsed/refractory metastatic triple-negative carcinoma (TNBC) who had received two or more prior systemic therapies (including a taxane), a minimum of one among them for metastatic disease. Randomization of patients to receive either Trodelvy or a chemotherapy chosen by the patients' treating physicians.

Important Safety Information for Trodelvy:

- NEUTROPENIA AND DIARRHEA
- Hypersensitivity and Infusion-Related Reactions
- Nausea and Vomiting
- Embryo-Fetal Toxicity

Conclusion:

- Breast cancer is a serious threat, especially in underdeveloped countries like India.
- ELI LILLY & Co. manufacture drug (Verzonia) which is indicated for HR+/HER2-. Roche manufacture drug (Kadcyla) for HR+/HER2- advanced breast cancer who have previously received Herceptin and taxane-based chemotherapy, either separately or together
- AstraZenca (Enhertu) for the treatment of adult patients with unresectable or metastatic HER2 negative/positive carcinoma who have received two or more prior anti-HER2 based regimens within the metastatic setting.
- Amongst all these biopharmaceutical companies Gilead Sciences (Trodelvy) is the only one indicated for TNAC. Trodelvy by adult patients receiving two or more prior systemic treatments for metastatic illness with locally advanced or metastatic triple negativity carcinoma (TNAC).
- Main goal is to cure cancer patients or prolong their life considerably, ensuring a good quality of life. To discover, develop and deliver innovative therapeutics for people with life-threatening diseases & to create a healthier world for all people.
- In the fight against breast cancer, screening mammograms are a powerful tool. Mammogram— X-ray pictures of the breast — can help reduce the number of deaths from breast cancer among women ages 40 to 70.

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Thank You

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