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Exploring the Efficacy of Targeted Therapies in Breast Cancer: A Comprehensive Review

Sittie Haynie Abdulatip[1], Sydney Mae Adorable[1], Shahah Shareen Agosila[1], Alexa Noreen Alforte[1], Nicole Dianne Aplaya[1], Vannyza Grace Cadion[1], Kristine Cahilig[1], and Jacqueline Padilla[2]

[1,2]San Pedro College, Davao City, Philippines
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A B S T R A C T

This article delves into the various treatments accessible for patients who are severely ill. It centers on how these remedies can assist in understanding the workings of breast cancer specifically. By utilizing such therapies, individuals learn to regulate their bodily reactions while cultivating beneficial practices and adjusting their mindset towards more favorable results. Although cancer patients initially show reluctance towards therapy to handle their mental health concerns related to critical illness, researchers believe that genetics in combination with environmental factors often lead to the emergence of Breast Cancer from various sources including behavioral aspects.

This leads to an increased risk manyfold over time due to certain hormone-catalyzed courses impacting individual behaviors. As it is one of the most frequently witnessed kinds worldwide and responsible for 12.5% of malignancy cases projected by year-end 2023, developing Breast Cancer remains primarily associated with being female whereby women are more vulnerable compared to counterparts' male healthcare population- supporting one out of four cancers carried by them. The incidence rate has progressively increased globally since its spurt nearly two decades ago, especially in localized-stage Hormone-receptor-positive diseases amounting to major causal elements. Despite positivity, decreasing death rates started showing itself at the 1989 peak trending slowly & stably downwards with a higher reduction trend around the preceding decade (1.5% vs 1/93%). Improvement seen can be attributed solely to enhanced medical interventions which have been dramatically successful over the years saving at least 390,000 individuals' lives at least.

The main objective currently gears toward targeting woman hormones promoting cell growth in an inbound inexhaustible quantity than males. Today claims without sufficient certainty - no proven prevention or treatment exists such as breast removal surgery as a definitive solution for women with heightened likelihoods of conjoining factually effective therapeutic procedures medically administered. Lessons learned from this research could be utilized to make patient lifelong comfort better by boosting survival rates using improved treatment methods available today.

Keywords: Targeted Therapies, Breast Cancer, Treatment, Hormonal Therapy, Receptor

1. Introduction

Breast cancer begins when there is an unusual growth of breast cells that generally starts in the ducts or lobules [1,4]. It is considered a cancer when it spreads to other parts of the body and can travel through blood and lymph arteries outside of the breast [1]. Breast cancer is a common illness that primarily affects women and individuals who were assigned female at birth (AFAB) [5]. It is characterized by the growth of tumors from malignant cells. It impacts men and assigned males at birth (AMAB), women 50 years of age and above, and younger AFAB. Invasion occurs in 80% of cases [2]. Lobular breast cancer, ductal carcinoma in situ (DCIS), and invasive ductal carcinoma (IDC) are among the prevalent types. Less common types include breast Paget's disease, inflammatory breast cancer, and triple-negative breast cancer (TNBC). Receptor cell status is used to categorize breast cancer subtypes, which aids in treatment planning for medical professionals. Estrogen receptors come in a variety of subtypes, including HER2-positive (HER2+), HR-positive (HR+), PR-positive (PR+), and HR-negative (HR-). PR+ and HR+ have progesterone and estrogen receptors, respectively, whereas HR-negative has no receptors [2,6,7].

Treatment for breast cancer varies based on its type and extent. A combination of surgical, chemotherapeutic, hormonal, biological, and radiation therapies is commonly employed. A key component of the all-encompassing treatment of breast cancer is the cooperative efforts of medical specialists from different specialties. [1,2,3,8]. Surgeons perform necessary operations, medical oncologists administer medications, and radiation oncologists oversee radiation therapy. By integrating these diverse therapeutic approaches, a more effective strategy can be formulated to combat the disease and manage potential side effects [3,9].

The development of focused medications has led to considerable advancements in the medical management of breast cancer [2,10,11,12,13]. These therapies focus on the distinctive attributes of cancer cells, such as the receptors they have or expressed genes, thereby enhancing therapy efficacy while

minimizing harm to healthy cells [1,5,14,15,16,17]. A notable form of targeted therapy involves the administration of medications that concentrate on the HER2 protein, such as trastuzumab (Herceptin), which demonstrates significant efficacy in treating HER2-positive breast tumors [2,6,7,18,19]. Another instance involves hormone treatment with drugs such as aromatase inhibitors or tamoxifen, which are employed in hormone receptor-positive breast malignancies to obstruct the impacts of estrogen or diminish its synthesis [20,21,22].

One type of targeted treatment is PARP inhibitors, primarily employed in breast cancer patients with BRCA1 or BRCA2 gene abnormalities [23,24,25,26]. These medications disrupt the cancer cells' capacity to mend their DNA, resulting in their demise. Furthermore, the utilization of CDK4/6 inhibitors, in conjunction with hormone therapy, has been effective in treating certain types of breast cancer by blocking the proteins that cause malignant cells to proliferate and spread [2,7,27,28,29].

The choice of targeted therapy is contingent upon the precise attributes of breast cancer, as ascertained through genetic and molecular testing [30,31,32]. By adopting a personalized approach to therapy, it is possible to implement more efficient and customized therapies, hence minimizing the likelihood of needless side effects and enhancing the overall outcome for the patient. The incorporation of targeted treatments into the treatment regimen emphasizes the significance of a multidisciplinary strategy, which includes oncologists, geneticists, and other healthcare experts, in effectively managing breast cancer [33,34,35].

2. Methods

This Article review uses multiple search engines such as PubMed, MedlinePlus, National Cancer Institute, breastcancer.org, mayoclicnic.org, Medscape, and WebMD to recover and explore the efficacy of targeted therapies in Breast Cancer. Analyzing the therapies found helped the researchers establish and review the different therapies used for breast cancer, and determine which drug exerts better efficacy for the different subtypes of breast cancer.

3. Pathogenesis of Breast Cancer

A woman's age, reproductive health, genetic predisposition, family history of breast cancer, and environmental exposure all enhance her risk of getting female breast cancer [36,37]. Factors related to procreation, including the number of children born, the age at which the first child is born, and caring, are equally significant as hormonal factors, which are mostly associated with the duration of estrogen exposure [38]. Genetic factors, the use of hormone replacement treatment, an unsuitable diet, and the accompanying obesity are all considered to play a crucial part in the development of breast cancer. Breast cancer develops in cells that line milk ducts and the lobules that feed milk to the ducts [39,40,41]. The basement membrane confines a carcinoma in situ to the ducts and lobules, where it is a non-invasive, early-stage proliferation of epithelial cells [42]. Based on the latest research, invasive breast cancers develop as a result of a series of molecular changes that occur at the cellular level. These changes result in immortal characteristics and unchecked proliferation in breast epithelial cells [43,44]. Genetic changes leading to unchecked cell proliferation in the mammary glands are usually initial signs in the development of breast cancer. These abnormal cells could develop into a tumor or localized mass. The cell benefits from these alterations in terms of selection, such as rapid development, and the progeny of a cell with one of these mutations will subsequently dominate the tumor population [45,46,47,48].

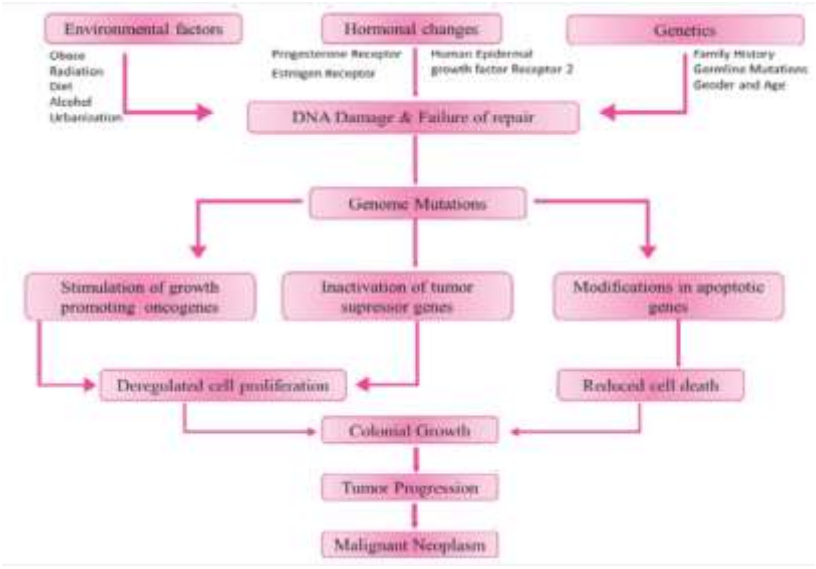

Figure 1: *The possible factors and pathophysiology of breast cancer. Adopted from Snijesh VP and Manoj R Kumar (2017)*

4. Targeted Therapies in Breast Cancer

One type of cancer treatment called targeted therapy focuses on particular proteins that control the development, proliferation, and metastasis of cancer cells. This approach forms the basis of precision medicine. With advancing knowledge of DNA alterations and cancer-driving proteins, researchers developed more effective treatments targeting these proteins. For advanced hormone receptor-positive breast cancer or breast cancer that has metastasized to other areas of the body, there are 25 different therapy choices. The starting of the targeted therapies is the **abemaciclib**. Belonging to the kinase inhibitor class, this medication functions by obstructing an abnormal protein that promotes the uncontrolled growth of cancerous cells [49]. This helps stop or slow the spread of malignant cells [49]. Secondly, **Ado-trastuzumab emtansine** Injection [50]. This is for Patients with HER2-positive metastatic breast cancer (cancer that has spread) who have not responded well to prior treatment with other medications (such as trastuzumab or taxane medication) or whose cancer has returned during or within six months of finishing treatment are candidates for adjuvant trastuzumab emtansine injection [50].

Anastrozole is a type of hormone medication that works by reducing the amount of estrogen produced by your body [51]. It is mostly advised for women with hormone-dependent breast cancer who have undergone menopause [51]. Fourth, **Elacestrant Dihydrochloride** [52]**.** Spread-related breast cancer and ER-positive/HER2-negative breast cancer including alterations in the ESR1 gene are among the types of breast cancers that have been approved to be treated with this drug [52]. It is designed for men and postmenopausal women whose disease has spread after being treated with at least one hormonal therapy [52]. Fifth, **Everolimus.** This medication belongs to a class of targeted therapies called mTOR inhibitors which block kinase proteins such as mTOR (mammalian target of rapamycin) [53]. When activated in certain cancers, mTOR causes them to grow out of control and make new blood vessels [53]. Some kinds of tumors can be stopped from growing further by using mTOR inhibitors [53].

Unlike traditional chemotherapy drugs, **exemestane** is not one of them. Instead, it is used in postmenopausal women who have finished their periods for both early and metastatic breast cancer [54]. It is often given to females who have previously taken tamoxifen as a cancer treatment [54]. Seventh is the targeted treatment drug called **Enhertu**. This drug with a chemical name, fam-trastuzumab-derux tecan-ki, works well against HER2-low breast cancer treated with chemotherapy; it also treats unresectable (not surgically removed) and metastatic HER2-positive breast cancer using an anti-HER2 medication [55]. The eighth kind is **faslodex**, not a chemotherapy but a hormonal therapy used to inhibit body estrogen receptors which cause breast cancer [56]. Patients with breast cancer can receive treatment with either faslodex alone or in combination with other drugs [56]. Ninth is **Lapatinib**. Solid tumors, especially lung and breast cancers, are treated using this drug developed by GSK (GlaxoSmithKline) [57]. The FDA approved its usage on March 13th, 2007 together with capecitabine which is a treatment for people with metastatic breast cancer that has progressed [57]. Both human epidermal growth factor receptor type 2 (HER2/ERBB2) and type 1 (HER1/EGFR/ERBB1) are inhibited by the tyrosine kinase drug lapatinib [57].

Olaparib is the tenth drug among the targeted therapies utilized for individuals with a particular kind of defective BRCA gene that is acquired or inherited [58]. This drug is used as a maintenance therapy for primary peritoneal cancer, fallopian tube cancer, and advanced ovarian cancer [58]. On the other hand, **Palbociclib** is the eleventh medication that is also effective in treating breast cancers [59]. It specifically targets HER2-negative, hormone receptor-positive, advanced-stage, or metastatic breast cancer in both men and women [59]. Unlike chemotherapy, IBRANCE, which is the active component of Palbociclib, functions to hinder cell proliferation in both healthy and cancerous cells [59]. Despite the potential for serious adverse effects, this treatment effectively slows down the progression of cancer [59]. Triple-negative breast cancer (TNBC) is a specific type of cancer that requires the use of **pembrolizumab** (Keytruda), a prescription drug classified as one of the twelve targeted therapies [60]. If the breast cancer has advanced or recurred, and it is not possible to remove it surgically, and the patient tests positive for "PD-L1" (programmed death ligand 1), cancer patients may consider incorporating keytruda alongside chemotherapy medications [60].

Perjeta, also known as pertuzumab, is the thirteenth medication on the list [61]. It is a prescription drug approved for use in patients with metastatic (HER2-positive) breast cancer who have not previously received chemotherapy or anti-HER2 therapy in combination with docetaxel and Herceptin® (trastuzumab) [61]. **Kisqali** ® (ribociclib) is another targeted treatment option for breast cancer. It functions as one of the targeted therapies by inhibiting or interfering with the chemicals involved in the growth of cancer cells [62]. Another type of targeted therapy for breast cancer is **Tucatinib** is a targeted (biological) treatment and is a member of the tyrosine kinase inhibitor class of cancer medications (TKIs) [63]. These targeted therapies disrupt cellular processes that contribute to the growth of cancer [63].

Alpelisib (Piqray) is a breast cancer therapy that belongs to a drug class of kinase inhibitors that functions by inhibiting the signals that contribute to the development of cancer cells [75]. This drug is used to treat HR+ and HER2- a type of breast cancer and has a mutation in the PIK3CA gene. PIK3CA-related overgrowth spectrum, or PROS, is a hereditary disorder that shows anomalies and overgrowth in specific body tissues. It is used together with fulvestrant to treat women who are going through the menopausal phase and men whose hormone therapy failed and resulted in the expansion and aggravation of their breast cancer [76]. Another drug for the treatment of breast cancer is **Capivasertib (Truqap),** which belongs to a drug class called serine/threonine kinase inhibitor [77]. It works similarly with alpelisib but with added function in the abnormal AKT2 or PTEN gene. It treats patients with hormone-treated breast cancer that has progressed and aggravated during or post-treatment, as well as patients who have experienced relapse within 12 months of mandatory adjuvant therapy [78].

Eighteenth on the list is **Letrozole (Femara),** which belongs to the drug class called nonsteroidal aromatase inhibitors that function by reducing the body's production of estrogen, resulting in slowing down or blocking specific types of cancerous cells that require estrogen [79]. This may be used along with other medications to treat menopausal women, HR+ breast cancer, and early-stage breast cancer with prior treatment of tamoxifen citrate for five years at least [80]. Another drug is **Margetixomab-cmkb (Matgenza),** which belongs to a class of medication known as monoclonal antibodies that inhibit the development of cancer cells [81]. Used to treat patients with HER2+ that has metastasized and for those who underwent two or more anti-

HER2 treatments [82]. The Twentieth drug is **Neratinib maleate (nerlynx),** it is a kinase inhibitor that treats HER2+ breast cancer patients [83,84]. It is given to patients receiving trastuzumab for early-stage breast cancer as an adjuvant therapy. Administered in conjunction with capecitabine to patients with metastatic or advanced cancer who had previously undergone two anti-HER2 treatments [84].

Sacituzumab govitecan-hziy (Trodelvy) is an antineoplastic drug used to treat patients with unresectable breast cancer, triple-negative cancer who went through two systemic treatments or more, HR+ and HER2- who were given a hormone treatment [85,86], in addition, this drug may also be used for unresectable and has propagated urothelial cancer in patients who received platinum chemotherapy and immunotherapy [85]. Another drug is **Talazoparib tosylate (Talzenna)** which belongs to a class of medication called poly (ADP-ribose) polymerase or PARP inhibitors [87]. Used to treat HER2- breast cancer and contains specific germline mutation in the BRCA1 or BRCA2 gene and is also used for the treatment of prostate cancer [88]. Placing the twenty-third drug is **Tamoxifen citrate (Soltamox)**. It is an antiestrogen used for the preventative treatment of women who have a high risk of acquiring breast cancer. It decreases the chance of acquiring invasive breast cancer and also functions as an adjuvant therapy in women who had surgery and radiation therapy [89,90].

Next is **Toremifene (fareston),** a nonsteroidal antiestrogen that inhibits the estrogen activity in the breast. It treats postmenopausal women whose breast cancer has progressed or metastasized and is ER+ or in cases where the type of cancer is unknown [91,93]. The last targeted therapy is called **Trastuzumab (Herceptin)**, which is a monoclonal antibody that treats HER2+, HR- or in patients with a high risk of acquiring cancer. It may be used in conjunction with other medications, such as doxorubicin hydrochloride and paclitaxel, to patients depending on what type of breast cancer they have [92,94].

5. Discussion

Several of these medicines have demonstrated promising outcomes in terms of their efficacy. Drugs such as Herceptin are particularly engineered to selectively target the hyperactive protein HER2, commonly found in specific subtypes of breast cancer. These medicines have the potential to decelerate or halt the proliferation of cancer cells, resulting in a favorable outcome [43, 45, 64, 65]. Nevertheless, it is crucial to take into account the potential adverse effects of these treatments. Targeted therapies, like other drugs, can induce undesirable effects. The negative effects might range from moderate to severe and may differ among individuals. Typical adverse effects encompass weariness, nausea, and dermatological issues [66, 67, 68].

Occasionally, more severe adverse effects may manifest. When evaluating the advantages vs. the disadvantages, it is akin to balancing the positives and negatives. Targeted therapy can exhibit significant efficacy in certain instances, potentially prolonging the lifespan of a patient with breast cancer. However, managing the negative effects can be difficult, and at times, they may surpass the advantages, particularly when the cancer is not aggressive [69]. Focused treatments for breast cancer have the potential to be efficacious in numerous instances; nonetheless, it is imperative to take into account the unique circumstances of each individual. It is advisable to visit a healthcare expert before deciding to utilize these therapies, considering the potential advantages and disadvantages for each patient. This is a continuously evolving field of study, with ongoing efforts to find novel treatments that enhance results and minimize adverse reactions [70, 71, 72].

A comprehensive approach is necessary to effectively treat early-stage breast cancer and prevent its recurrence. This entails focusing on the channels that encourage the proliferation and infiltration of cancerous cells. However, treatments for endocrine and cytostatic disorders may result in resistance, which reduces their efficacy. Clinical trials combining these treatments with inhibitors of the growth factor pathway or its downstream signaling elements are necessary to overcome this. By doing so, it can improve the quality of care provided to patients with breast cancer. Molecular targeted therapy has long involved targeting the estrogen receptor (ER), and over the past 25 years, tamoxifen has greatly improved cure rates, quality of life, and disease prevention.

Various medications have been identified as targeted therapies for breast cancer patients. Studies have shown that these treatments can prolong the lifespan of patients, allowing them to live longer. These medications have undergone testing and modifications, making them suitable for both short-term and long-term use. Breast cancer is a complicated illness where several factors influence the growth and spread of cancer cells. Targeted therapies act as a defense mechanism against the rapid progression and spread of these malignant cells. By inhibiting the growth potential of cancer cells, targeted therapies disrupt the specific mechanisms that drive the disease, ultimately preserving the overall health of the patient. Targeted medicines have emerged as a powerful tool in the battle against breast cancer, offering the potential of precision medicine and improved patient outcomes.

6. Conclusion

Surgery is usually the first line of treatment for breast cancer, followed by chemotherapy, hormone therapy, or radiation. To conclude this article review, there are 25 targeted therapies for breast cancer targeting different subtypes of the disease. For the treatment of ER+ and HER2- are **Elacestrant Dihydrochloride** and **Abemaciclib**, the latter exerts the best efficacy for that type of breast cancer; there are four drugs for the treatment of HER2+, namely **Lapatinib, Mergetixomab-cmkb (Matgenza), Tucatinib, Perjata, and Ado-Trastuzumab emtansine** (kadcyla), in which kadcyla is the drug of choice; **Anastrazole and Faslodex** for hormone therapy with **Faslodex** having increased efficacy; **Everolimus and Exemestane** are crucial for addressing both advanced (late-stage) cancer or noncancerous tumors and early/advanced breast cancer in postmenopausal women, respectively; **Enhertu** works against unresectable, HER2+ with previous treatment of anti-HER2 medicine, and HER2-low breast cancer with prior therapy of chemotherapy; In conjunction with chemotherapy, PARP inhibitors such as **Pembrolizumab** (Keytruda), **Olaparib**, and **Talazoparib tosylate** (Talzenna) are used to treat triple-negative breast cancer. Keytruda is the recommended medication for this kind of breast cancer; **Palbociclib** targets HER2-, HR+, advanced-stage, or metastatic breast cancer in both men and women; another drug is the **Kisqali** that treats HR+, HER2- metastatic breast cancer; **Alpelisib** (Piqray)

and **Capivasertib** (Truqap) addresses specific mutations in the PIK3CA gene while **Letrozole** (Femara) stands out for its versatility in treating postmenopausal women with HR+ early-stage breast cancer; Monoclonal antibodies **Margetuximab-cmkb (**Margenza) and **Trastuzumab** (Herceptin) demonstrate the progress made in precision medicine against HER2+ metastatic breast cancer, while **Neratinib Maleate** (Nerlynx) and **Sacituzumab ovitecan-hziy** (Trodelvy) provide breakthroughs in adjuvant therapy and unresectable triple-negative breast cancer, respectively; **Talazoparib Tosylate** (Talzenna) a poly (ADP-ribose) polymerase inhibitor highlights efficacy in HER2-negative cases with BRCA1 or BRCA2 mutations; **Tamoxifen Citrate** (Soltamox) and **Toremifene** (Fareston) contributes to metastatic breast cancer and risk reductions strategies. To summarize, from the article title itself, these targeted therapies exert the best efficacy depending on the different types of receptors they target to treat various subtypes of breast cancer.

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REFERENCES:

1. Centers for Disease Control and Prevention. What Is Breast Cancer? Centers for Disease Control and Prevention, https://www.cdc.gov/cancer/breast/basic_info/what-is-breast-cancer.htm (2023, accessed December 6, 2023).
2. Professional CCM. Breast Cancer. Cleveland Clinic, https://my.clevelandclinic.org/health/diseases/3986-breast-cancer.
3. How Is Breast Cancer Treated? Centers for Disease Control and Prevention, https://www.cdc.gov/cancer/breast/basic_info/treatment.htm (2023).
4. Eldridge L. How Fast Does Breast Cancer Start, Grow, and Spread? Verywell Health, https://www.verywellhealth.com/breast-cancer-growth-rate-4175666 (2023).
5. Breast cancer - Symptoms and causes - Mayo Clinic. Mayo Clinic, https://www.mayoclinic.org/diseases-conditions/breast-cancer/symptoms-causes/syc-20352470 (2022).
6. Lobular Carcinoma In Situ (LCIS). National Breast Cancer Foundation, https://www.nationalbreastcancer.org/types-of-breast-cancer/ (2020).
7. Types of Breast Cancer. Memorial Sloan Kettering Cancer Center, https://www.mskcc.org/cancer-care/types/breast/types-breast.
8. Łukasiewicz S, Czeczelewski M, Forma A, et al. Breast Cancer—Epidemiology, Risk Factors, Classification, Prognostic Markers, and Current Treatment Strategies—An Updated Review. Cancers 2021; 13: 4287.
9. Wilkinson N, Zuckerman R. Surgical Oncology for the General Surgeon. Surgical Clinics of North America 2020; 100: i.
10. Advancing Cancer Therapy. Nature Cancer; 245–246. Epub ahead of print on March 24, 2021. DOI: 10.1038/s43018-021-00192-x.
11. Debela DT, Muzazu SG, Heraro KD, et al. New approaches and procedures for cancer treatment: Current perspectives. SAGE Open Medicine 2021; 9: 205031212110343.
12. Pucci C, Martinelli C, Ciofani G. Innovative approaches for cancer treatment: current perspectives and new challenges. ecancermedicalscience; 13. Epub ahead of print September 10, 2019. DOI: 10.3332/ecancer.2019.961.
13. Ruggeri B. Cancer 2021: New therapeutic approaches for the treatment of cancer — building on advances in cancer biology and the molecular genetics of cancer. Current Opinion in Pharmacology 2021; 60: 341–345.
14. Allen GM, Lim WA. Rethinking cancer-targeting strategies in the era of smart cell therapeutics. Nature Reviews Cancer; 693–702. Epub ahead of print September 29, 2022. DOI: 10.1038/s41568-022-00505-x.
15. Zhang Y, Zhang Z. The history and advances in cancer immunotherapy: understanding the characteristics of tumor-infiltrating immune cells and their therapeutic implications. Cellular & Molecular Immunology; 807–821. Epub ahead of print July 1, 2020. DOI: 10.1038/s41423-020-0488-6.
16. Mensurado S, Blanco-Domínguez R, Silva-Santos B. The emerging roles of γδ T cells in cancer immunotherapy. Nature Reviews Clinical Oncology; 178–191. Epub ahead of print January 9, 2023. DOI: 10.1038/s41571-022-00722-1.
17. Kumar AR, Devan AR, Nair B, et al. Harnessing the immune system against cancer: current immunotherapy approaches and therapeutic targets. Molecular Biology Reports 2021; 48: 8075–8095.

18. Targeted Drug Therapy | Breast Cancer Treatment. American Cancer Society, https://www.cancer.org/cancer/types/breast-cancer/treatment/targeted-therapy-for-breast-cancer.html.
19. Swain SM, Shastry M, Hamilton E. Targeting HER2-positive breast cancer: advances and future directions. Nature Reviews Drug Discovery; 101–126. Epub ahead of print November 7, 2022. DOI: 10.1038/s41573-022-00579-0.
20. Hormone Therapy for Breast Cancer. WebMD, https://www.webmd.com/breast-cancer/breast-cancer-hormone-therapy-choices (2004).
21. Hormone Therapy for Breast Cancer Fact Sheet. National Cancer Institute, https://www.cancer.gov/types/breast/breast-hormone-therapy-fact-sheet (2022).
22. Almstedt K, Schmidt M. Targeted Therapies Overcoming Endocrine Resistance in Hormone Receptor-Positive Breast Cancer. Breast Care 2015; 10: 168–172.
23. Cortesi L, Rugo HS, Jackisch C. An Overview of PARP Inhibitors for the Treatment of Breast Cancer. Targeted Oncology; 255–282. Epub ahead of print on March 12, 2021. DOI: 10.1007/s11523-021-00796-4.
24. Tung N, Garber JE. PARP inhibition in breast cancer: progress made and future hopes. npj Breast Cancer; 8. Epub ahead of print on April 8, 2022. DOI: 10.1038/s41523-022-00411-3.
25. Rose M, Burgess JT, O'Byrne K, et al. PARP Inhibitors: Clinical Relevance, Mechanisms of Action and Tumor Resistance. Frontiers in Cell and Developmental Biology; 8. Epub ahead of print September 9, 2020. DOI: 10.3389/fcell.2020.564601.
26. Repairing DNA Damage in Cancer Cells. Memorial Sloan Kettering Cancer Center, https://www.mskcc.org/news/repairing-dna-damage-cancer-cells (2022).
27. Alhmoud JF, Woolley JF, Al Moustafa A-E, et al. DNA Damage/Repair Management in Cancers. Cancers 2020; 12: 1050.
28. Majidinia M, Yousefi B. DNA repair and damage pathways in breast cancer development and therapy. DNA Repair 2017; 54: 22–29.
29. Targeted Therapy for Cancer. National Cancer Institute, https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies (2022).
30. Targeted Therapy. MD Anderson Cancer Center, https://www.mdanderson.org/treatment-options/targeted-therapy.html.
31. Professional CCM. Targeted Therapy. Cleveland Clinic, https://my.clevelandclinic.org/health/treatments/22733-targeted-therapy.
32. Montoya S, Soong D, Nguyen N, et al. Targeted Therapies in Cancer: To Be or Not to Be, Selective. Biomedicines 2021; 9: 1591.
33. Zhou Z, Li M. Targeted therapies for cancer. BMC Medicine; 20. Epub ahead of print March 11, 2022. DOI: 10.1186/s12916-022-02287-3.
34. Zhou Z, Li M. Targeted therapies for cancer. BMC Medicine; 20. Epub ahead of print March 11, 2022. DOI: 10.1186/s12916-022-02287-3.
35. Cancer Therapy and Oncology International Journal (CTOIJ), https://juniperpublishers.com/ctoij/CTOIJ.MS.ID.555672.php.
36. Dogara G, Saud SMB, Kamin Y bin, et al. Developing Soft Skills through Project Based Learning in Technical and Vocational Institutions. International Journal of Engineering and Advanced Technology 2019; 9: 2842–2847.
37. Parenthood and Procreation (Stanford Encyclopedia of Philosophy), https://plato.stanford.edu/entries/parenthood/ (2021).
38. Mahmoud R, Kimonis V, Butler MG. Genetics of Obesity in Humans: A Clinical Review. International Journal of Molecular Sciences 2022; 23: 11005.
39. Loos RJF, Yeo GSH. The genetics of obesity: from discovery to biology. Nature Reviews Genetics; 120–133. Epub ahead of print September 23, 2021. DOI: 10.1038/s41576-021-00414-z.
40. Hinney A, Körner A, Fischer-Posovszky P. The promise of new anti-obesity therapies arising from knowledge of genetic obesity traits. Nature Reviews Endocrinology; 623–637. Epub ahead of print July 28, 2022. DOI: 10.1038/s41574-022-00716-0.
41. Targeted Cancer Therapy | Targeted Drug Therapy for Cancer. American Cancer Society, https://www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy/what-is.html.
42. Gatza ML, Lucas JE, Barry WT, et al. A pathway-based classification of human breast cancer. Proceedings of the National Academy of Sciences of the United States of America; 6994–6999. Epub ahead of print March 24, 2010. DOI: 10.1073/pnas.0912708107.
43. Blows FM, Driver KE, Schmidt MK, et al. Subtyping of Breast Cancer by Immunohistochemistry to Investigate a Relationship between Subtype and Short and Long Term Survival: A Collaborative Analysis of Data for 10,159 Cases from 12 Studies. PLoS Medicine 2010; 7: e1000279.
44. The Cell: A Molecular Approach. 2nd Edition. 2000.

45. Taurin S, Alkhalifa H. Breast cancers, mammary stem cells, and cancer stem cells, characteristics, and hypotheses. Neoplasia 2020; 22: 663–678.

46. Chen W, Wei W, Yu L, et al. Mammary Development and Breast Cancer: a Notch Perspective. Journal of Mammary Gland Biology and Neoplasia 2021; 26: 309–320.

47. Feng Y, Spezia M, Huang S, et al. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. Genes & Diseases 2018; 5: 77–106.

48. Professional CCM. Lobular Breast Cancer (Invasive Lobular Carcinoma). Cleveland Clinic, https://my.clevelandclinic.org/health/diseases/21180-lobular-breast-cancer.

49. Abemaciclib: MedlinePlus Drug Information [Internet]. medlineplus.gov. Available from: https://medlineplus.gov/druginfo/meds/a617049.html

50. Kadcyla. www.breastcancer.org. Available from https://www.breastcancer.org/treatment/targeted-therapy/kadcyla

51. Anastrozole (Oral Route) Description and Brand Names - Mayo Clinic [Internet]. www.mayoclinic.org. Available from: https://www.mayoclinic.org/drugs-supplements/anastrozole-oral-route/description/drg-20061868

52. Elacestrant Dihydrochloride - NCI [Internet]. www.cancer.gov. 2023 [cited 2023 Dec 19]. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/elacestrant-dihydrochloride

53. Everolimus: Uses, Dosage, Side Effects, Warnings [Internet]. Drugs.com. Available from: https://www.drugs.com/everolimus.html

54. Exemestane: MedlinePlus Drug Information [Internet]. medlineplus.gov. Available from: https://medlineplus.gov/druginfo/meds/a607006.html

55. Jaber N. Enhertu Approved for Lung Cancer - NCI [Internet]. www.cancer.gov. 2022. Available from: https://www.cancer.gov/news-events/cancer-currents-blog/2022/fda-lung-cancer-enhertu-her2

56. Faslodex Injection: Uses, Dosage, Side Effects, Warnings [Internet]. Drugs.com. Available from: https://www.drugs.com/faslodex.html

57. Lapatinib: MedlinePlus Drug Information [Internet]. medlineplus.gov. Available from: https://medlineplus.gov/druginfo/meds/a607055.html

58. Lynparza (olaparib) dosing, indications, interactions, adverse effects, and more [Internet]. reference.medscape.com. Available from: https://reference.medscape.com/drug/lynparza-olaparib-999934

59. Ibrance [Internet]. www.breastcancer.org. Available from: https://www.breastcancer.org/treatment/targeted-therapy/ibrance

60. Flynn JP, Gerriets V. Pembrolizumab [Internet]. Nih.gov. StatPearls Publishing; 2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546616/

61. Perjeta (Pertuzumab): Side Effects, How it Works, and More [Internet]. www.breastcancer.org. Available from: https://www.breastcancer.org/treatment/targeted-therapy/perjeta

62. Kisqali (ribociclib): Side Effects, How it Works, and More [Internet]. www.breastcancer.org. Available from: https://www.breastcancer.org/treatment/targeted-therapy/kisqali

63. Reynolds S. Tucatinib Approved for HER2-Positive Colorectal Cancer - NCI [Internet]. www.cancer.gov. 2023. Available from: https://www.cancer.gov/news-events/cancer-currents-blog/2023/fda-tucatinib-her2-colorectal-cancer

64. Holland K. What Is HER2 FISH Testing? Healthline, https://www.healthline.com/health/breast-cancer/her2-fish (2020).

65. Goldberg JF. Special Report: Guidance on Managing Side Effects of Psychotropics. Psychiatric News; 56. Epub ahead of print on August 1, 2021. DOI: 10.1176/appi.pn.2021.8.30.

66. Fu S, Zhao Q. Quantitation and Identification of Therapeutic Anti-CD22 Monoclonal Antibodies in a Cell-Based ELISA Method. Antibodies 2022; 11: 53.

67. APA PsycNet, https://psycnet.apa.org/fulltext/2021-45656-002.html.

68. Targeted Drug Therapy. American Cancer Society, https://www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html.

69. Leicht L. How to Handle Tricky Questions About Your Metastatic Breast Cancer, https://www.healthcentral.com/slideshow/how-to-handle-tricky-questions-about-metastatic-breast-cancer?ap=808&kw=breast%20cancer%20options&mt=p&pcid=531023973&adsetid=1355700351682935&msclkid=be6913ca996b1c103f8776a5ef59e803 (2023).

70. Lau KH, Tan AM, Shi Y. New and Emerging Targeted Therapies for Advanced Breast Cancer. International Journal of Molecular Sciences 2022; 23: 2288.

71. Gautam N, Elleson KM, Ramamoorthi G, et al. Current State of Cell Therapies for Breast Cancer. The Cancer Journal 2022; 28: 301–309.

72. Genes and Cancer. Cancer.Net, https://www.cancer.net/navigating-cancer-care/cancer-basics/genetics/genes-and-cancer (2023).

73. Enhertu [Internet]. www.breastcancer.org. Available from: https://www.breastcancer.org/treatment/targeted-therapy/enhertu

74. BCRF. Triple-Negative Breast Cancer: Treatment, Symptoms, Research | BCRF [Internet]. Breast Cancer Research Foundation. 2023 [cited 2023 Dec 20]. Available from: https://www.bcrf.org/blog/triple-negative-breast-cancer-treatment-symptoms-research/#:~:text=Immunotherapy%20agents%20(such%20as%20atezolizumab

75. Alpelisib: MedlinePlus Drug Information [Internet]. medlineplus.gov. Available from: https://medlineplus.gov/druginfo/meds/a619036.html

76. Alpelisib - NCI [Internet]. www.cancer.gov. 2019. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/alpelisib

77. Capivasertib [Internet]. go.drugbank.com. Available from: https://go.drugbank.com/drugs/DB12218

78. Capivasertib - NCI [Internet]. www.cancer.gov. 2023 [cited 2023 Dec 21]. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/capivasertib

79. Letrozole: MedlinePlus Drug Information [Internet]. medlineplus.gov. Available from: https://medlineplus.gov/druginfo/meds/a698004.html#:~:text=Letrozole%20is%20in%20a%20class

80. Letrozole - National Cancer Institute [Internet]. www.cancer.gov. 2006. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/letrozole

81. Margetuximab-cmkb Injection: MedlinePlus Drug Information [Internet]. medlineplus.gov. [cited 2023 Dec 21]. Available from: https://medlineplus.gov/druginfo/meds/a621004.html#:~:text=Margetuximab%2Dcmkb%20is%20in%20a

82. Margetuximab-cmkb - NCI [Internet]. www.cancer.gov. 2021. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/margetuximab-cmkb

83. Neratinib: MedlinePlus Drug Information [Internet]. medlineplus.gov. [cited 2023 Dec 21]. Available from: https://medlineplus.gov/druginfo/meds/a617034.html#:~:text=Neratinib%20is%20in%20a%20class

84. Neratinib Maleate - NCI [Internet]. www.cancer.gov. 2017 [cited 2023 Dec 21]. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/neratinibmaleate

85. Sacituzumab Govitecan-hziy - NCI [Internet]. www.cancer.gov. 2020. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/sacituzumabgovitecan-hziy

86. Sacituzumab Govitecan-Hziy (Intravenous Route) Description and Brand Names - Mayo Clinic [Internet]. www.mayoclinic.org. [cited 2023 Dec 21]. Available from: https://www.mayoclinic.org/drugs-supplements/sacituzumab-govitecan-hziy-intravenous-route/description/drg-20488176#:~:text=Sacituzumab%20govitecan%2Dhziy%20belongs%20to

87. Talazoparib: MedlinePlus Drug Information [Internet]. medlineplus.gov. [cited 2023 Dec 21]. Available from: https://medlineplus.gov/druginfo/meds/a618070.html#:~:text=Talazoparib%20is%20in%20a%20class

88. Talazoparib Tosylate - NCI [Internet]. www.cancer.gov. 2019 [cited 2023 Dec 21]. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/talazoparibtosylate

89. Tamoxifen: MedlinePlus Drug Information [Internet]. medlineplus.gov. Available from: https://medlineplus.gov/druginfo/meds/a682414.html#:~:text=Tamoxifen%20is%20in%20a%20class

90. Tamoxifen Citrate - National Cancer Institute [Internet]. www.cancer.gov. 2006. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/tamoxifencitrate

91. Toremifene: MedlinePlus Drug Information [Internet]. medlineplus.gov. [cited 2023 Dec 21]. Available from: https://medlineplus.gov/druginfo/meds/a608003.html#:~:text=Toremifene%20is%20in%20a%20class

92. Trastuzumab Intravenous: Uses, Side Effects, Interactions, Pictures, Warnings & Dosing - WebMD [Internet]. www.webmd.com. [cited 2023 Dec 21]. Available from: https://www.webmd.com/drugs/2/drug-16623/trastuzumab-intravenous/details

93. Toremifene - NCI [Internet]. www.cancer.gov. 2009 [cited 2023 Dec 21]. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/toremifene

94. Trastuzumab - National Cancer Institute [Internet]. www.cancer.gov. 2006. Available from: https://www.cancer.gov/about-cancer/treatment/drugs/trastuzumab