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Pertuzumab in Her2 Positive Breast Cancer: Review

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ABSTRACT
Pertuzumab is a monoclonal antibody that has shown significant efficacy in the treatment of HER2-positive breast cancer. It functions by preventing the human epidermal growth factor receptor, or HER2, from dimerizing. The combination of trastuzumab and pertuzumab has increased the survival rates of HER2-positive breast cancer in both early and advanced stages. However, some individuals have experienced disease relapse, making resistance to therapy a difficulty. The goal of ongoing research is to find trustworthy indicators of HER2-targeted therapeutic sensitivity and resistance, as this could result in more individualized treatment plans. Future paths for treatment of HER2-positive breast cancer include developing pertuzumab as a tailored therapeutic option and resolving any issues with T-DXd (trastuzumab deruxtecan) use in clinical settings. The potential of pertuzumab in treating HER2-positive breast cancer is promising and could lead to more effective treatments for this disease.

I. INTRODUCTION

Overview of HER2 positive breast cancer

Human epidermal growth factor receptor 2 (HER2) is a protein that is overexpressed in HER2-positive breast cancer, a subtype of breast cancer (1). An more aggressive form of breast cancer and unchecked cell proliferation may result from this overabundance. Twenty percent or so of all breast cancers are HER2-positive(2), (3). The good news is that HER2-positive breast cancer cells can now be specifically targeted with targeted therapies like trastuzumab (Herceptin), which improves treatment results for those with this subtype (2).Determining the HER2 status of an individual is crucial for treatment planning as it aids in selecting the most advantageous medications for those with this particular form of breast cancer (2). Fast-growing invasive breast cancer that is likely to spread (metastasize) from the breast to other parts of the body is known as HER2-positive breast cancer (3). On the other hand, if HER2-positive breast cancer is detected early on, doctors can frequently effectively treat it(3).It's crucial to remember that although HER2-positive breast cancer behaves more aggressively and grows much faster than other types of cancer, it also has a far higher propensity to react favourably to medications that target the HER2 protein(1).

Importance of targeted therapies in HER2-positive breast cancer

The treatment of HER2-positive breast cancer has undergone a revolution due to targeted therapies, which have also significantly improved disease control and survival rates (2).About 15% to 20% of all breast tumors are HER2-positive, meaning that their cells have a lot of the protein HER2 on their surface (4). This protein is a crucial regulator of cell division and viability (4). By focusing on this protein in particular, targeted medicines are intended to treat HER2-positive breast tumors (5) (4).The ability of targeted therapies to function even in the absence of chemotherapy is one of their main advantages (5). They may also improve the efficacy of other forms of therapy (5). For instance, compared to chemotherapy alone, the chance of recurrence is halved for those with HER2-positive early breast cancer who receive chemotherapy plus trastuzumab (a targeted therapy)(4).In addition, the side effect profile of targeted therapies differs from that of chemotherapy. They don't affect bone marrow, induce nausea or vomiting, or cause hair loss (4). Heart health is continuously monitored during treatment, though, as they have the potential to cause major cardiac issues (4).In summary, because targeted therapies can precisely target cancer cells,

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enhance the effectiveness of other treatments, and have a more favorable side effect profile than conventional chemotherapy, they are essential in the treatment of HER2-positive breast cancer (4)(5)(1).

Introduction to Pertuzumab and its role in treating HER2-positive breast cancer

Pertuzumab, marketed under the brand name Perjeta®, is a humanized anti-HER2 monoclonal antibody(6). It plays a important role in the treatment of HER2-positive breast cancer by reducing the proliferation and survival of HER2-positive breast cancer cells(6).Pertuzumab works by inhibiting the dimerization of HER receptors on the cell surface, which is a key step in receptor-mediated mitogenic signaling(6). This mechanism is complementary to that of another anti-HER2 drug, trastuzumab(7). Pertuzumab binds to a different site on the HER2 receptor than trastuzumab, allowing the two drugs to work synergistically(6).In clinical trials, Pertuzumab has shown significant benefits when used in combination with trastuzumab and chemotherapy(8). It has been found to prolong both progression-free survival and overall survival in patients with HER2-positive metastatic breast cancer(8). Moreover, Pertuzumab has been shown to increase pathological complete response rates and produce high 3-year survival rates when used as part of neoadjuvant therapy(6).Pertuzumab is indicated as first-line treatment for metastatic or recurrent HER2-positive breast cancer, in combination with trastuzumab and docetaxel(6). It is also indicated as neoadjuvant treatment of locally advanced, inflammatory, or high-risk early-stage disease, in combination with trastuzumab plus docetaxel or chemotherapy(6).In conclusion, Pertuzumab plays a vital role in the treatment of HER2-positive breast cancer due to its unique mechanism of action and its ability to work synergistically with other treatments to improve patient outcomes(6)(7)(8).

Mechanism Of Action of Pertuzumab

Pertuzumab is a recombinant humanized monoclonal antibody that targets the extracellular dimerization domain (subdomain II) of the human epidermal growth factor receptor 2 protein (HER2)(9)(10).The mechanism of action of Pertuzumab involves blocking the dimerization of HER2 with other HER family members(9)(11)(10). Dimerization is a process where two HER2 receptors pair up, which is a key step in receptor-mediated signaling that promotes cell growth and proliferation(9)(10)(11). By inhibiting this process, Pertuzumab halts cell growth and initiates apoptosis (programmed cell death)(9)(11)(12).This mechanism is unique and complementary to that of another anti-HER2 drug, trastuzumab, which binds to a different site on the HER2 receptor(9). This allows the two drugs to work synergistically, enhancing the effectiveness of treatment for HER2-positive breast cancer(9).

Pertuzumab in Combination Therapy

Combination of Transtuzamb and Pertuzumab

The combination of trastuzumab and pertuzumab has been a significant advancement in the treatment of HER2-positive breast cancer(13)(14).Trastuzumab and pertuzumab are both monoclonal antibodies that target the HER2 receptor, but they bind to different sites on the receptor, allowing them to work synergistically(13). This means that the combined effect of using the two molecules is far greater than when using either alone(13).The Food and Drug Administration (FDA) approved a new fixed-dose combination of pertuzumab, trastuzumab, and hyaluronidase–zzxf (PHESGO, Genentech, Inc.) for subcutaneous injection for the treatment of HER2-positive breast cancer(14). This combination is used with chemotherapy as neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early-stage breast cancer(14). It is also used as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence(14). Furthermore, it is used in combination with docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease(14).Clinical trials have shown that the combination of IV pertuzumab, IV trastuzumab, and chemotherapy leads to improved outcomes in patients with HER2-positive breast cancer versus IV trastuzumab plus chemotherapy alone(14).

In conclusion, the combination of trastuzumab and pertuzumab has proven to be a highly effective treatment strategy for HER2-positive breast cancer, offering improved outcomes and survival rates for patients(13)(14).

Comparison of safety and efficacy of combined therapy with monotherapy

The combination of trastuzumab and pertuzumab has been shown to be more effective than pertuzumab monotherapy in the treatment of HER2-positive breast cancer(15,16).In terms of efficacy, studies have shown that dual therapy significantly improved overall survival (OS) and

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progression-free survival (PFS) in advanced breast cancer compared to monotherapy(16). For instance, end-of-study analyses of the CLEOPATRA trial found a median overall survival of 57.1 months in patients receiving pertuzumab combined with trastuzumab compared with 40.8 months in control patients, a benefit of 16.3 months(15).In terms of safety, both therapies have been associated with adverse events, but the combination of trastuzumab and pertuzumab has not been shown to significantly increase the risk of adverse events compared to pertuzumab alone(15). However, it's important to note that all treatments can have side effects and the risk of side effects should always be weighed against the potential benefits of the treatment[1].In conclusion, the combination of trastuzumab and pertuzumab has been shown to be more effective than pertuzumab alone in the treatment of HER2-positive breast cancer, without a significant increase in the risk of adverse events(17)(18).

Clinical trials and studies

There have been several clinical trials and studies conducted to evaluate the efficacy and safety of Pertuzumab in the treatment of HER2-positive breast cancer. Here are some key studies:

1. **CLEOPATRA Trial**: This was a double-blind, randomized, placebo-controlled, phase 3 study(19). The end-of-study analyses found a median overall survival of 57.1 months in patients receiving pertuzumab compared with 40.8 months in control patients, a benefit of 16.3 months(17).
2. **Comparative Effectiveness and Safety Study**: This study compared the effectiveness and safety of Pertuzumab and Trastuzumab plus chemotherapy vs Trastuzumab plus chemotherapy for the treatment of metastatic breast cancer(17).
3. **P013 Study**: This was a randomized, phase III, equivalency clinical trial that compared the efficacy and safety of a proposed pertuzumab biosimilar with the reference pertuzumab(20).
4. **Real-World Effectiveness Study**: This study investigated whether the benefit on pathological complete response (pCR) seen in clinical trials is confirmed in a real-world setting(21).

These studies have provided valuable insights into the effectiveness and safety of Pertuzumab in treating HER2-positive breast cancer. However, more research is needed to further understand the long-term effects and potential uses of this drug.

Discussion on the results of these trials and their implications

1. **CLEOPATRA Trial**: The final prespecified overall survival analysis in the phase III CLEOPATRA study showed a significant 15.7-month increase in median overall survival over 50 months of follow-up with the addition of pertuzumab to trastuzumab and docetaxel in the first-line treatment of women with HER2-positive metastatic breast cancer(22). This trial demonstrated that the combination of pertuzumab, trastuzumab, and chemotherapy significantly improved progression-free survival and overall survival in patients with HER2-positive metastatic breast cancer(22)(23).
2. **Comparative Effectiveness and Safety Study**: This study compared the effectiveness and safety of Pertuzumab and Trastuzumab plus chemotherapy vs Trastuzumab plus chemotherapy for the treatment of metastatic breast cancer(17). The study found that the combination of pertuzumab, trastuzumab, and chemotherapy led to improved outcomes in patients with HER2-positive breast cancer versus trastuzumab plus chemotherapy alone.

Adverse effects and safety profile

Adverse effects associated with Pertuzumab

Pertuzumab, like any medication, can cause side effects. Here are some of the common and serious side effects associated with Pertuzumab:

Common Side Effects(24):

- Diarrhea
- Nausea
- Vomiting
- Fatigue
- Mucositis (inflammation of the lining of the digestive tract)
- Myelosuppression (reduction in bone marrow activity)
- Infection
- Bleeding
- Dysgeusia (distorted sense of taste)
- Rash
- Pruritus (itching)
- Anorexia (loss of appetite)
- Weight loss
- Infusion-related reaction
- Paresthesia (abnormal sensation of the skin)

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- Hair loss or thinning of the hair
- Loss of taste
- Nasal congestion
- Redness or soreness around the fingernails

Serious Side Effects(25):

- Black, tarry stools
- Burning, numbness, tingling, or painful sensations
- Chills
- Cough
- Fast heartbeat
- Fever
- Hives, itching, or rash
- Hoarseness
- Joint pain, stiffness, or swelling
- Lower back or side pain
- Painful or difficult urination
- Pale skin
- Redness of the skin
- Sore throat
- Swelling of the eyelids, face, lips, hands, or feet
- Tightness in the chest
- Troubled breathing or swallowing
- Ulcers, sores, or white spots in the mouth
- Unsteadiness or awkwardness
- Unusual bleeding or bruising
- Unusual tiredness or weakness
- Weakness in the arms, hands, legs, or feet.

Safety profile of Pertuzumab

Pertuzumab is a targeted therapy used in the treatment of **HER2-positive breast cancer**. Here's what we know about its safety profile:

1. **Clinical Trials**:
   - In a **phase 3 randomized clinical trial** conducted in **Asian patients**, adding pertuzumab to trastuzumab and docetaxel resulted in a **significant improvement** in **pathologic complete response (pCR)** rates compared to placebo, trastuzumab, and docetaxel(26).
   - The safety data aligned with the **known pertuzumab safety profile**.
   - Another study found that pertuzumab, when added to trastuzumab and docetaxel, had an **acceptable tolerability profile** and did not increase cardiac toxicity(15).
2. **Real-World Experience**:
   - Real-world data also support the use of pertuzumab. Neoadjuvant treatment with pertuzumab and trastuzumab achieved **high pCR rates** in patients with HER2-positive early breast cancer, demonstrating an **acceptable safety profile**(21).
3. **FDA Approval**:
   - The FDA approved pertuzumab for **adjuvant treatment** of HER2-positive breast cancer based on its safety and efficacy data.
   - While the safety profile is generally acceptable, caution is advised for patients aged ≥65 years due to observed toxicity(27).

In summary, pertuzumab, when combined with trastuzumab and docetaxel, has shown efficacy and an acceptable safety profile in the treatment of HER2-positive breast cancer. Always consult with your healthcare provider for personalized information.

II. DISCUSSION

Ongoing research and Future directions for the use of Pertuzumab

Pertuzumab is a monoclonal antibody that has been used in the treatment of HER2-positive breast cancer. It works by inhibiting the dimerization of HER2, a human epidermal growth factor receptor(19).Ongoing research is focused on identifying reliable biomarkers of sensitivity and resistance to HER2-targeted therapy, which would make possible the individualization of treatment for patients with HER2-positive breast cancer(19). There are also ongoing clinical trials assessing novel HER2-targeted agents as third-line therapy or beyond for HER2-positive advanced breast cancer(28). Future directions include the development of pertuzumab as a personalized therapeutic option for HER2-positive breast cancer[3], and addressing potential challenges related to the use of T-DXd (trastuzumab deruxtecan) in clinical practice(29). The most robust overall response rate (62.0%) and median duration of response (18.2 months) were observed for trastuzumab-deruxtecan among heavily pretreated patients(28).

In conclusion, the ongoing research and future directions in the use of pertuzumab are promising and could potentially lead to more effective and personalized treatments for HER2-positive breast cancer.

III. CONCLUSION

Pertuzumab is a monoclonal antibody that plays a significant role in the treatment of HER2-positive breast cancer. It works by inhibiting HER2, a human epidermal growth factor receptor, by binding to a different HER2 epitope than

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trastuzumab(7). This represents a complementary mechanism of action to trastuzumab(7).

The efficacy and safety of pertuzumab in combination with trastuzumab, with or without chemotherapy, have been demonstrated in both advanced and early stages of HER2-positive breast cancer(7). In patients with HER2-positive metastatic breast cancer, pertuzumab added to trastuzumab and docetaxel has been shown to significantly prolong both progression-free survival and overall survival(8).

The potential of pertuzumab in treating HER2-positive breast cancer is being explored in ongoing research. For instance, a first-in-human PET study on patients with HER2-positive breast cancer evaluated the safety, biodistribution, and dosimetry of 89 Zr-site-specific (ss)-pertuzumab PET(30). The study demonstrated the potential clinical applications of 89 Zr-ss-pertuzumab PET/CT(30).

In conclusion, pertuzumab has a significant role in the treatment of HER2-positive breast cancer and its potential is being further explored in ongoing research.

REFERENCES

[1]. Breast Cancer HER2 Status | What is HER2 Status? [Internet]. [cited 2024 Jun 10]. Available from: https://www.cancer.org/cancer/types/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-her2-status.html

[2]. Breast Cancer: Ask Health Professionals [Internet]. [cited 2024 Jun 10]. Available from: https://microsoftstart.msn.com/en-us/health/ask-professionals/in-expert-answers-on-breastcancer/in-breastcancer?questionid=zm33u0dd&type=condition&source=bingmainline_conditionqna

[3]. HER2-Positive Breast Cancer: Symptoms & Treatment [Internet]. [cited 2024 Jun 10]. Available from: https://my.clevelandclinic.org/health/diseases/25213-her2-positive-breast-cancer

[4]. Targeted Therapies for HER2-Positive Early Breast Cancer | Susan G. Komen® [Internet]. [cited 2024 Jun 11]. Available from: https://www.komen.org/breast-cancer/treatment/type/her2-targeted-therapies/trastuzumab/

[5]. Targeted Drug Therapy | Breast Cancer Treatment [Internet]. [cited 2024 Jun 11]. Available from: https://www.cancer.org/cancer/types/breast-cancer/treatment/targeted-therapy-for-breast-cancer.html

[6]. McCormack PL. Pertuzumab in HER2-positive breast cancer: a guide to its use. Drugs Ther Perspect. 2016 Feb 1;32(2):35–41.

[7]. Cortes J, Moya-Horno I. The expanding role of pertuzumab in the treatment of HER2-positive breast cancer. Breast Cancer Targets Ther. 2015 May;125.

[8]. Von Minckwitz G, Procter M, De Azambuja E, Zardavas D, Benyunes M, Viale G, et al. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med. 2017 Jul 13;377(2):122–31.

[9]. Pertuzumab [Internet]. [cited 2024 Jun 11]. Available from: https://go.drugbank.com/drugs/DB06366

[10]. Pertuzumab (PERJETA®) | Available Agents | NCI Formulary [Internet]. [cited 2024 Jun 11]. Available from: https://nciformulary.cancer.gov/available_agents/Pertuzumab.htm

[11]. Pertuzumab_monograph.pdf [Internet]. [cited 2024 Jun 11]. Available from: http://www.bccancer.bc.ca/drug-database-site/Drug%20Index/Pertuzumab_monograph.pdf

[12]. Pertuzumab: Dosage, Mechanism/Onset of Action, Half-Life - Medicine.com [Internet]. [cited 2024 Jun 11]. Availablefrom:https://www.medicine.com/drug/pertuzumab/hcp

[13]. Fuentes G, Scaltriti M, Baselga J, Verma CS. Synergy between trastuzumab and pertuzumab for human epidermal growth factor 2 (Her2) from colocalization: an in silicobased mechanism. Breast Cancer Res. 2011 May 22;13(3):R54.

[14]. FDA Approves Fixed-Dose Pertuzumab/Trastuzumab Combo in HER2+ Breast Cancer [Internet]. [cited 2024 Jun 11]. Available from: https://www.onclive.com/view/fda-approves-fixed-dose-pertuzumab-trastuzumab-combo-in-her2-breast-cancer

[15]. McCormack PL. Pertuzumab in HER2-positive breast cancer: a guide to its use. Drugs Ther Perspect. 2016 Feb 1;32(2):35–41.

[16]. Liu X, Fang Y, Li Y, Li Y, Qi L, Wang X. Pertuzumab combined with trastuzumab compared to trastuzumab in the treatment

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 654-660 www.ijprajournal.com ISSN: 2456-4494

of HER2-positive breast cancer: A systematic review and meta-analysis of randomized controlled trials. Front Oncol [Internet]. 2022 Sep 28 [cited 2024 Jun 7];12. Available from: https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2022.894861/full

[17]. Comparative Effectiveness and Safety of Pertuzumab and Trastuzumab Plus Chemotherapy vs Trastuzumab Plus Chemotherapy for Treatment of Metastatic Breast Cancer | Oncology | JAMA Network Open | JAMA Network [Internet]. [cited 2024 Jun 11]. Available from: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2789454

[18]. Frontiers | Pertuzumab combined with trastuzumab compared to trastuzumab in the treatment of HER2-positive breast cancer: A systematic review and meta-analysis of randomized controlled trials [Internet]. [cited 2024 Jun 11]. Available from: https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2022.894861/full

[19]. Pertuzumab and Its Accelerated Approval: Evolving Treatment Paradigms and New Challenges in the Management of HER2-Positive Breast Cancer [Internet]. [cited 2024 Jun 11]. Available from: https://www.cancernetwork.com/view/pertuzumab-and-its-accelerated-approval-evolving-treatment-paradigms-and-new-challenges-management

[20]. Allahyari A, Ehsanpour A, Najafi B, Ansarinejad N, Mehrzad V, Kalantari B, et al. Comparing efficacy and safety of P013, a proposed pertuzumab biosimilar, with the reference product in HER2-positive breast cancer patients: a randomized, phase III, equivalency clinical trial. BMC Cancer. 2022 Sep 7;22(1):960.

[21]. González-Santiago S, Saura C, Ciruelos E, Alonso JL, de la Morena P, Santisteban Eslava M, et al. Real-world effectiveness of dual HER2 blockade with pertuzumab and trastuzumab for neoadjuvant treatment of HER2-positive early breast cancer (The NEOPETRA Study). Breast Cancer Res Treat. 2020 Nov 1;184(2):469–79.

[22]. CLEOPATRA Overall Survival Analysis: Significant Benefit for Pertuzumab Plus Trastuzumab/Docetaxel in HER2-Positive Metastatic Breast Cancer - The ASCO Post [Internet]. [cited 2024 Jun 11]. Available from: https://ascopost.com/issues/may-25-2015/cleopatra-overall-survival-analysis-significant-benefit-for-pertuzumab-plus-trastuzumabdocetaxel-in-her2-positive-metastatic-breast-cancer/

[23]. Stenger M. End-of-Study Results From CLEOPATRA: Pertuzumab, Trastuzumab, and Docetaxel in HER2-Positive Metastatic Breast Cancer [Internet]. [cited 2024 Jun 11]. Available from: https://ascopost.com/news/march-2020/end-of-study-results-from-cleopatra/

[24]. RxList [Internet]. [cited 2024 Jun 11]. Pertuzumab-Trastuzumab-Hyaluronidase: Side Effects, Uses, Dosage, Interactions, Warnings. Available from: https://www.rxlist.com/pertuzumab-trastuzumab-hyaluronidase/generic-drug.htm

[25]. Pertuzumab Side Effects: Common, Severe, Long Term [Internet]. [cited 2024 Jun 11]. Available from: https://www.drugs.com/sfx/pertuzumab-side-effects.html

[26]. Efficacy, Safety, and Tolerability of Pertuzumab, Trastuzumab, and Docetaxel for Patients With Early or Locally Advanced ERBB2-Positive Breast Cancer in Asia: The PEONY Phase 3 Randomized Clinical Trial | Breast Cancer | JAMA Oncology | JAMA Network [Internet]. [cited 2024 Jun 11]. Available from: https://jamanetwork.com/journals/jamaoncology/fullarticle/2753172

[27]. FDA Approval Summary: Pertuzumab for Adjuvant Treatment of HER2-Positive Early Breast Cancer | Clinical Cancer Research | American Association for Cancer Research [Internet]. [cited 2024 Jun 11]. Available from: https://aacrjournals.org/clincancerres/article/25/10/2949/10666/FDA-Approval-Summary-Pertuzumab-for-Adjuvant

[28]. Simmons C, Rayson D, Joy AA, Henning JW, Lemieux J, McArthur H, et al. Current and future landscape of targeted therapy in HER2-positive advanced breast cancer: redrawing the lines. Ther Adv Med Oncol. 2022 Jan 1;14:17588359211066677.

[29]. Ali A, Graff SL. Exploring DESTINY: the Past, Present, and Future of Trastuzumab

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 654-660 www.ijprajournal.com ISSN: 2456-4494

Deruxtecan. Curr Oncol Rep. 2024 Jan 1;26(1):1–9.

[30]. Yeh R, O'Donoghue JA, Jayaprakasam VS, Mauguen A, Min R, Park S, et al. First-in-Human Evaluation of Site-Specifically Labeled 89Zr-Pertuzumab in Patients with HER2-Positive Breast Cancer. J Nucl Med [Internet]. 2024 Jan 25 [cited 2024 Jun 11]; Available from: https://jnm.snmjournals.org/content/early/2024/01/25/jnumed.123.266392