Dual Anti-HER2 Combination with Chemotherapy as First-line Treatment for HER2-positive Metastatic Breast Cancer

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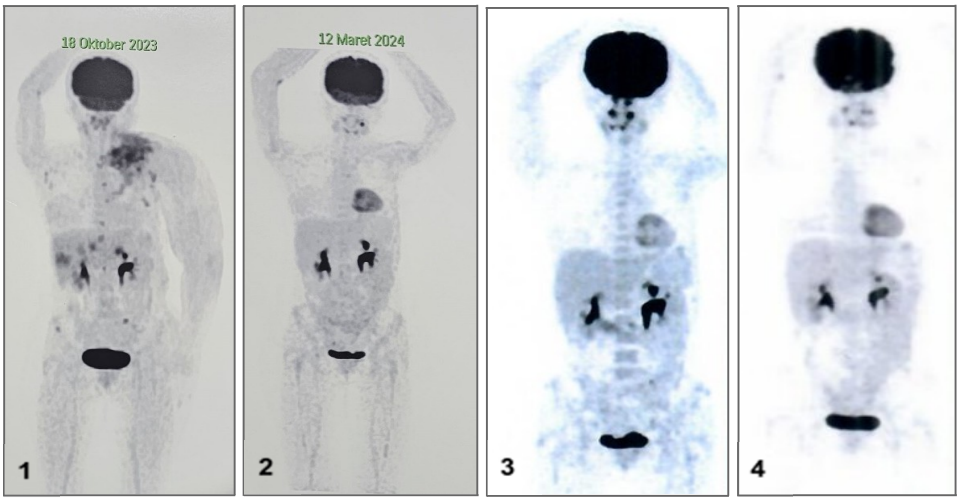

Figure 1. (1) Pretreatment PET scan showed soft tissue swelling with dilated blood vessels in the left anterior cervical region, subcutaneous thickening with multiple hypermetabolic lesions at the left musculus pectoralis major consistent with relapsed left breast carcinoma. Additionally, hypermetabolic multiple lymph nodes were observed in the left axilla, posterior cervical, pectoral, and supra-infraclavicular regions, with metastasis to the liver and bones. (2) After six cycles of Pertuzumab, Trastuzumab, and Docetaxel, the PET scan showed the disappearance of hypermetabolic lesions associated with relapsed left breast carcinoma. There were no hypermetabolic multiple lymph nodes or liver nodules; however, blastic lesions with lower metabolic activity were still present in the sternum and left sacrum, indicating a good response to treatment. (3) After continuing Pertuzumab and Trastuzumab for six cycles, the PET scan revealed stable disease, indicating a favorable response to the treatment. (4) A follow-up PET scan after five months showed stable disease and no visible disease progression.

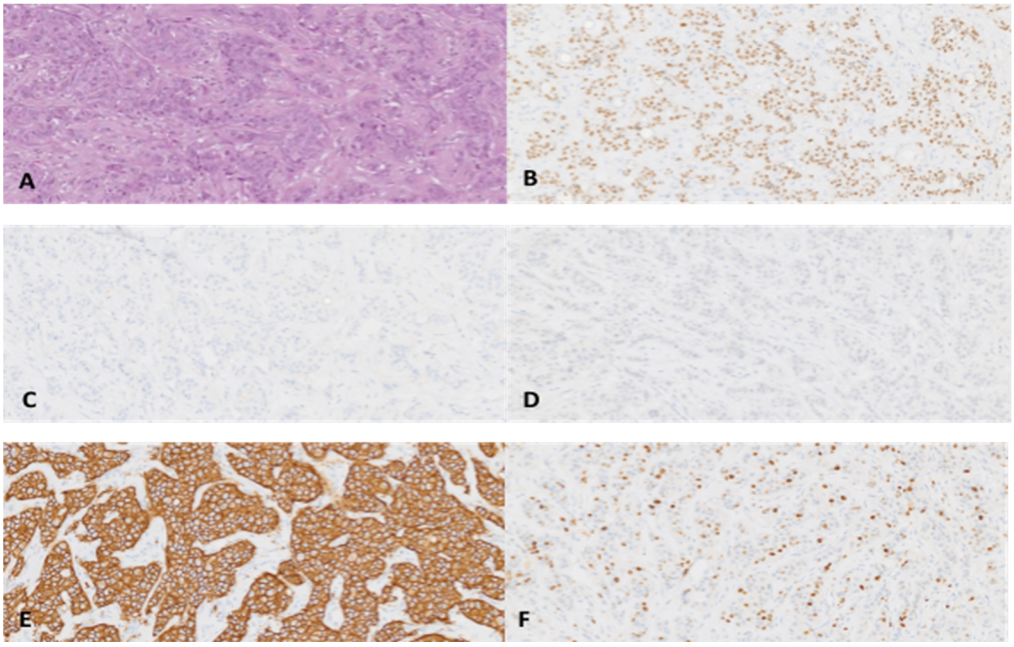

Figure 2. Metastatic carcinoma in the axilla (A), confirmed to originate from breast cancer by diffuse nuclear GATA3 staining (B). The tumor shows negative immunostaining for estrogen receptor and progesterone receptor (C, D), strong HER2 membrane positivity (E), and Ki67 30% (F).

Human epidermal growth factor receptor 2 (HER2)-overexpressing breast cancer is an aggressive subtype of breast cancer associated with a higher likelihood of recurrence, metastasis, and mortality. HER2-positive breast cancer accounts for approximately 15%–20% of all breast cancer cases, with 4%–9% of patients presenting with metastatic disease at the time of initial diagnosis. Furthermore, 20%–30% of early-stage HER2-positive breast cancer cases progress to metastatic disease.[1]

The overexpression of HER2 plays an important role in the development and progression of this breast cancer subtype. HER2-positive metastatic breast cancer is associated with chemotherapy resistance and exhibits a poor prognosis, characterized by high rates of recurrence and mortality when chemotherapy is administered without anti-HER2 agents.[2] According to phase 3 of the Clinical Evaluation of Pertuzumab and Trastuzumab (CLEOPATRA) trial, the combination of dual anti-HER2 therapy–Trastuzumab and Pertuzumab–and Docetaxel has been approved by the FDA as the first-line treatment of HER2-positive metastatic breast cancer.[3] Herein, we report a case of a patient with metastatic HER2-positive left breast cancer who achieved a great therapeutic response with a combination of dual anti-HER2 and chemotherapy.

A 50-year-old woman with a history of left mastectomy in 2019 was concerned about undergoing adjuvant chemotherapy and radiotherapy. Three years later, she presented it to the outpatient clinic of hematology-medical oncology in October 2023 with erythematous skin changes, a nodule in the mastectomy area, and lymphedema of her left arm. An excisional biopsy of the nodule was performed, which confirmed an invasive carcinoma characterized as ER− PR− HER2+ breast cancer. A PET scan was performed and showed a relapse of left breast carcinoma with metastatic involvement of multiple lymph nodes, liver, and bone. The patient was diagnosed with metastatic left breast cancer (Ca mammae sinistra) cT4cN3cM1 ER−, PR−, HER2+.

The patient was treated with a combination of Pertuzumab, Trastuzumab, and Docetaxel administered every 3 weeks for six cycles. Therapeutic response evaluation via PET scan demonstrated a good response, characterized

by the complete resolution of relapsed left breast carcinoma, multiple lymph nodes, and liver lesions, along with substantial regression of bone metastases. Maintenance therapy with Pertuzumab and Trastuzumab was continued for an additional six cycles. A subsequent PET scan evaluation demonstrated an excellent outcome, indicating a stable disease. Pertuzumab and Trastuzumab therapy were continued every 3 weeks until disease progression was observed.

The development of HER2-targeted therapies has significantly transformed the natural course of HER2-positive metastatic breast cancer (mBC), markedly improving progression-free survival (PFS) and overall survival (OS). For patients experiencing relapses within 1 year after completing adjuvant therapy or those with de novo HER2-positive mBC, the combination of Pertuzumab, Trastuzumab, and Docetaxel is the preferred first-line treatment regimen, as supported by findings from the CLEOPATRA trial. In this phase III trial, the median PFS was 12.4 months (95% CI: 10–14) in the placebo group and 18.7 months (95% CI: 17–22) in the Pertuzumab group (HR 0.69, 95% CI: 0.59–0.81). At the 5-year landmark analysis, the OS rates were 49% (95% CI: 44–54) in the Pertuzumab group and 35% (95% CI: 30–40) in the placebo group. Furthermore, the end-of-study analysis of CLEOPATRA showed that 37% of patients who continued therapy with Pertuzumab and Trastuzumab were alive after more than 8 years of follow-up.[3,4]

Trastuzumab binds to subdomain 4 of the HER2 extracellular domain, activating antibody-dependent cellular cytotoxicity and cellular phagocytosis. This mechanism effectively downregulates HER2 activity and inhibits HER2-overexpressing tumor cells. Conversely, Pertuzumab binds to subdomain 2 of HER2, thereby inhibiting the overexpression of HER2. The combination of Trastuzumab and Pertuzumab demonstrates enhanced antitumor efficacy by providing dual inhibition of HER2.[5]

CONCLUSION

We observed a case of HER2-positive recurrent left breast cancer with metastatic involvement of multiple lymph nodes, liver, and bones, demonstrating a significant therapeutic response to a combination of Pertuzumab, Trastuzumab, and Docetaxel. These outcomes align with the findings of the CLEOPATRA trial, highlighting the pivotal role of dual anti-HER2 therapy combined with chemotherapy in improving the survival outcomes of patients with metastatic HER2-positive breast cancer.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare

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