Title

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Journal

Proceedings of UCLA Health, 23(1)

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Publication Date

2020-03-13

CASE REPORT

Postoperative Therapy after Partial Response to Neoadjuvant Treatment of HER2 Positive Breast Cancer

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Case Report

A 52-year-old postmenopausal woman underwent a screening mammogram which revealed architectural distortion of the left breast. Subsequent diagnostic mammogram and ultrasound demonstrated a 21 mm mass in the upper outer quadrant of the left breast. Biopsy revealed grade 2 invasive ductal carcinoma, Estrogen Receptor (ER) positive, Progesterone Receptor (PR) positive, ki67 high at 50%, HER 2 positive at 3+ by immunohistochemistry (IHC). Subsequent MRI of the breast confirmed a 22 mm mass in the left breast upper outer quadrant. She was felt to have clinical stage IIA T2N0M0 breast cancer.

This patient was treated with neoadjuvant docetaxel, carboplatin, trastuzumab and pertuzumab (TCHP) for 6 cycles. Subsequently she chose to undergo bilateral mastectomies and was found to have residual 1.8 cm low grade invasive ductal carcinoma with chemotherapy effect seen. Three sentinel nodes were removed, none involved with carcinoma- residual ypT1cN0M0 disease. Her systemic therapy then continued with ado-trastuzumab emtansine (T-DM1) and anastrazole.

Discussion

Neoadjuvant therapy is often used in the setting of HER2 positive breast cancer due to high rates of clinical and pathologic response to the combination of chemotherapy and HER 2 blocking agents. Neoadjuvant therapy was used in this patient to allow her time to make a decision about her surgical options, and also to guide adjuvant therapy decisions based on her pathologic response to neoadjuvant treatment. In addition, if she had undergone mastectomy as her first treatment and was found to have nodal involvement, she likely would have undergone an axillary node dissection. Therefore neoadjuvant therapy can potentially minimize nodal surgery by clearing microscopic nodal involvement.

The combination of chemotherapy and HER2 blockade is standard neoadjuvant treatment for most stages of HER 2 positive disease. In September 2013, the FDA granted accelerated approval to pertuzumab as neoadjuvant therapy in combination with trastuzumab and docetaxel for stage II or higher breast cancer based on the NeoSphere Trial.[1] In this trial, patients received 4 cycles of neoadjuvant docetaxel with trastuzumab, pertuzumab, or both, and patients in one additional arm of the trial received the antibodies alone, trastuzumab and pertuzumab, without docetaxel. The addition of pertuzumab to docetaxel and trastuzumab resulted in a higher pathologic complete response rate (pCR)- 46% versus 29%. Patients receiving pertuzumab and trastuzumab without docetaxel had a pCR rate of only 17%, demonstrating the importance of chemotherapy in the treatment of HER2 positive breast cancer. Based on the results of the NeoSphere trial, pertuzumab is routinely incorporated into the neoadjuvant treatment of stage II or higher HER2 positive breast cancer.

An additional multi-arm trial, the TRYPHAENA trial,[2] evaluated neoadjuvant TCHP, as well as chemotherapy with an anthracycline-containing chemotherapy regimen combined with trastuzumab and pertuzumab initiated either concurrently or after the anthracycline. The results demonstrated pCR rates exceeding 55% on all arms, with the TCHP regimen resulting in a 64% pCR, although this study was not powered for comparison between the arms. The non-anthracycline containing TCHP regimen has been adopted by many oncologists as standard of care, felt to be equally effective but less toxic than anthracycline-based regimens.

In an attempt to improve on outcomes with neoadjuvant therapy in HER2 positive disease, the Kristine Trial[3] compared neoadjuvant T-DM1 plus pertuzumab to TCHP. Although the T-DM1 combination therapy was better tolerated with fewer serious adverse events, the pathologic response rate to TCHP exceeded that of the T-DM1 arm (55.7 vs 44.4%) and therefore chemotherapy combined with HER2 blockade remains the standard of care in the neoadjuvant setting.

In contrast to the Kristine Trial, the adjuvant use of T-DM1 compared to trastuzumab on the Katherine Trial[4] did show an improvement in 3-year invasive disease free survival with T-DM1 (88 vs 77%) in women with HER2-positive early breast cancer with residual invasive disease after neoadjuvant chemotherapy and trastuzumab. Therefore current standard of care is to give T-DM1 postoperatively if the patient does not achieve a pCR following TCHP or other neoadjuvant therapy, while trastuzumab with or without pertuzumab is recommended treatment after a pCR.

Patients presenting with stage I HER 2 positive breast cancer, were evaluated in a phase II study[5] of weekly paclitaxel for 12 weeks in combination with 1 year of trastuzumab. This resulted in excellent 7-year disease free survival rates of 94.6% in

hormone receptor positive patients and 90.7% in hormone negative patients. Therefore, for clinical stage I disease, although neoadjuvant therapy can be implemented as it does give prognostic information and can potentially change adjuvant therapy, surgery as the first treatment modality is also an option. If the disease is truly stage I, the well-tolerated and effective adjuvant regimen of paclitaxel and trastuzumab alone can be used.

For the patient discussed above, T-DM1 was administered postoperatively as she did not achieve a pCR after neoadjuvant therapy. In addition, she will also be treated with an aromatase inhibitor for her hormone receptor positive breast cancer.

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