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The updated use of dual HER2 blockade in breast cancer therapy: A project of an institutional experience

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According to SEER database, more than 3 million women live with breast cancer worldwide. A recent statistical analysis evaluated the incidence and prevalence of breast cancer in Lebanese women, and revealed that it was the most prevalent cancer in Lebanon, accounting for 20% of all cancer cases, among the highest in the world. The average age-standardized incidence rate over 11 years (2005-2015) was 96.5 per 100,000, with a significantly increasing trend over time [1]. The adherence to the most recent guidelines in the treatment of breast cancer in the Lebanese population is a must, in order to obtain the best outcomes in terms of remission and survival.

The last decade witnessed an unprecedented revolution in the treatment of breast cancer, especially with the approval of dual Human Epidermal growth factor Receptor 2 (HER2) blockade in the neoadjuvant treatment of tumors expressing the HER2-Neu receptor [2].

We aim to review our registry of women with breast cancer at Hôtel-Dieu de France university hospital and evaluate outcomes in patients who received dual HER2 blockade in association with chemotherapy for the neoadjuvant treatment of HER-2 positive breast cancer and compare our data to international ones.

Trastuzumab and Pertuzumab in combination with chemotherapy for the neoadjuvant treatment of HER2-positive breast cancer: what is the evidence?

The HER2 receptor overexpression is known to label breast cancer with a worse prognosis [3]. The successful use of transtuzumab (a monoclonal antibody that blocks the HER2 receptor by blocking its cleavage and inhibiting intracellular signaling) in combination with chemotherapy in the adjuvant treatment of operable HER2-positive breast cancer was a turning point in the management of this group of patients [4]. Pertuzumab is a novel humanized monoclonal antibody directed at the dimerization domain of HER2, a different binding site than trastuzumab, and has an additional effect on HER2-HER3 heterodimerization [5]. This suggested that the activity of pertuzumab might be complementary to that of trastuzumab, and the drug was first approved in 2012 for the first-line treatment of patients with metastatic HER2-positive breast cancer in combination with trastuzumab and chemotherapy on the basis of the CLEOPATRA trial that proved its efficacy. In fact, this combination provided a median overall survival of 56.5 months, a duration that was rarely reached before pertuzumab in metastatic breast cancer patients expressing the HER2-Neu receptor, who were previously known to have a "bad disease" [6].

In 2013, The U.S. Food and Drug Administration (FDA) granted accelerated approval to pertuzumab in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of patients with early stage breast cancer, based on the NeoSphere trial. This was a multicenter, open-label, phase II study that randomized treatment-naive women with locally advanced, inflammatory, or early stage HER2-positive breast cancer to receive one of four neoadjuvant regimens: the combination of pertuzumab or trastuzumab, or both, with docetaxel and the combination of pertuzumab and trastuzumab without chemotherapy. NeoSphere demonstrated that the percentage of pathological complete remission (pCR) achieved was significantly superior in those who received pertuzumab in combination with trastuzumab (45·8%) and docetaxel than those given trastuzumab plus docetaxel (29·0%), without substantial differences in tolerability [7]. The safety of a dual HER2 blockade in the neoadjuvant treatment of breast cancer was further reinforced by TRYPHAENA, a randomized phase II cardiac safety study [8]. Results of TRYPHAENA were also more promising since it reported a pCR of 81% with the addition of pertuzumab in the group of patients with HER2-positive and hormone receptor-negative breast cancer. Subsequently, 5-year analysis of NeoSphere data supported the previous findings, and despite not finding a statistically significant survival benefit, suggested that pCR could be an early indicator of long-term outcome in early-stage HER2-positive breast cancer, because patients who achieved this target in all groups combined had longer progression-free survival (85% [76-91]) compared with patients who did not (76% [71-81]) [9]. Moreover, starting 2019, the minority of patients who do not achieve a complete remission with neoadjuvant taxane and trastuzumab-based therapy can be offered an adjuvant treatment with ado-trastuzumab emtansine based on the KATHERINE trial [10].

Dual HER2 blockade in combination with chemotherapy for the neoadjuvant treatment of HER2-positive breast cancer: a project of real world experience

Based on the above data, all women with breast cancer must be exposed to the latest available therapeutic options to get the maximal benefit. In our institution, Hôtel-Dieu de France hospital, we offer the above approved combination where indicated.

Our project is to retrospectively collecting data of all women diagnosed with operable HER2-positive breast cancer who received the combination of trastuzumab and pertuzumab with chemotherapy in the neoadjuvant setting, evaluate the pathological response in these patients, and compare our rate of pCR to that reported in the literature.

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We will collect the reported adverse events during treatment course and address toxicity as a secondary endpoint.

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