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Neoadjuvant Chemotherapy in Triple Negative Breast Cancer Patients

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ABSTRACT

The only breast cancer (BC) subtype without targeted therapies is triple negative breast cancer (TNBC), which makes for 15–20% of incident breast cancers. TNBC is HER2 (human epidermal growth factor receptor 2) negative using clinical tests, and immunostaining reveals a negligible (1%) expression of ER and PR. It has the most dismal prognosis of all BC subtypes due to its biologically aggressive tumor, which is characterized by moderate/high grade and highly proliferating cancer cells. Although invasive ductal carcinoma is the most frequent presentation of TNBC, there are specific TNBC histologies that require special attention due to differing biology and prognosis.[3] Patients with operable illness are increasingly receiving neoadjuvant chemotherapy, which was formerly reserved for patients with locally progressed or inflamed breast cancer, notably in TNBC patients. More people can have breast-conserving surgery (BCS) thanks to this therapeutic strategy, which also assesses how well it is working.[1] An important prognostic factor with positive long-term results is achieving a pathological complete response (pCR). A higher pCR rate is related to the delivery of NACT regimens with platinum salts. However, at the expense of confusing treatment recommendations there is higher incidence of negative outcomes.[4] Improvements in pathologic complete response rates and patient outcomes in the neoadjuvant setting are the main topics of clinical research.[1]

Keywords: Triple negative breast cancer, Neoadjuvant Chemotherapy, pCR.

INTRODUCTION

Breast cancer has been classified as a heterogeneous disease with multiple subtypes that respond differently to various medicines as a result of advancements in genetic research. Perou and colleagues[5] used gene expression profiling to identify 4 subtypes of breast tumors, including ER-positive luminal-like, basal-like (BL), human epidermal growth factor receptor 2 (HER2)-positive, and normal breast tumors, providing the first explanation of the notion of sub typing breast tumors. According to the current American Society of Clinical Oncology (ASCO) and College of American Pathologists guidelines[6], oestrogen and progesterone negativity is defined as less than 1% of tumor cells staining. Triple negative breast cancer (TNBC) is typically defined as the absence of oestrogen, progesterone, and HER2 receptors (ER-negative, progesterone receptor [PR]-negative, and HER2-negative).[6] TNBCs that are histopathologically assessed are typically, but not always, BL (around 85%). As a result, despite the fact that they are not the same thing, TNBCs are frequently mistakenly thought of as the same thing as the BL subtype.

Neoadjuvant chemotherapy was initially intended to be used in patients with locally advanced disease in order to transform inoperable tumors into operable tumors. Neodjuvant chemotherapy is defined as the administration of systemic therapy prior to surgical removal of a breast tumour. Neoadjuvant chemotherapy's importance in raising the prevalence of conservation therapy and the related decreased morbidity and improved self-image have been fully recognized since the advent of this concept. Meanwhile, delays in surgery for patients who are resistant to neoadjuvant chemotherapy and local control following tumor downstaging have raised concerns. But the outcomes of a randomized clinical trial comparing the efficacy of neoadjuvant chemotherapy with adjuvant chemotherapy in patients with operable breast cancer were comparable. 5500 women who qualified for this analysis were used in this paper. Additionally, it was revealed that 25% of patients avoid mastectomy due to neoadjuvant chemotherapy. While receiving neoadjuvant chemotherapy, however, about 5% of the patients who were initially candidates for conservation therapy needed a mastectomy due to cancer progression.[7]

TRIPLE NEGTIVE BREST CANCER

Breast cancer (BC) affected 1.7 million women globally in 2012, and 521,900 of them lost their lives to the disease. These numbers cover all BC subtypes, yet it is common knowledge that BC is not a uniform condition. Genomic research has revealed four main intrinsic subtypes: basal-like (BL) BC, HER2-positive BC, and the luminal subtypes A and B, which express hormone receptor-related genes. The heterogeneous category known as triple-negative BC (TNBC) is distinguished by the absence of HER2 over-expression and the absence of hormone receptor expression. The research does not agree on the definition of a negative oestrogen receptor (ER) status by immunohistochemistry (IHC), and other definitions only consider ER expression to be important if at least 10% of tumor cells express the receptors. TNBC is defined as BC with less than 1% of tumor cells expressing the ER and progesterone receptors via IHC by the St Gallen guidelines, the American Society of Clinical Oncology[5], and the American College of Pathology. TNBC makes for 15% of all BCs and is distinguished by a poorer overall survival rate and an early peak in distant recurrences at 3 years following diagnosis. The majority of deaths take place within the first five years of a diagnosis. With this BC subtype, late tumor recurrences are uncommon, and recurrences are typically not seen after 8 years.[10] TNBC exhibits an aggressive clinical course and is more likely to experience local and distant relapses, which frequently manifest as visceral and/or brain metastases. TNBCs usually belong to the intrinsic subset of BCs known as the BL molecular phenotype in microarray-based expression profiling study. On gene expression arrays, not all TNBCs have a BL molecular phenotype, nevertheless. In fact, BL tumors make about 75–80% of TNBCs. High-molecular-weight basal cytokeratin 5/6 (CK5/6), CK14, B crystallin, CK17, epidermal growth factor receptor (EGFR), HER1, caveolin 1/2 (CAV1/2), vimentin, fascin, c-Kit, and P-cadherin are a few markers that have been found by IHC in tumor cells and are also present in normal basal/myoepithelial cells of the breast.E-cadherin and other epithelial markers are less likely to be expressed in TNBC. Similar to TNBC, not all BL BCs are TNBC; up to 54% of BL BCs lack a TN phenotype on IHC. It's true that some BL malignancies over-express HER2 or express ER. Only chemotherapy (CT) is currently the standard of care for individuals with TNBC, while in certain nations bevacizumab is still given to CT in advanced BC (ABC), despite the lack of any evidence that doing so improves overall survival. To find aims that can be achieved, however, extensive study is still being done. There are numerous clinical studies being conducted to enhance the results of the existing medical

paradigm. A better understanding of the biology of this BC subgroup will enable us to assess novel targeted therapeutic strategies for this challenging disease.[9]

INCIDENCE AND CLINICAL PRESENTATION

TNBCs are categorized as 10% to 17% of breast cancers based on ER, PR, and HER2 immune histochemical staining. Despite their generally aggressive character, TNBCs are less likely to metastasis to the axillary lymph nodes, according to multiple studies. TNBCs are more likely to metastatically spread to the brain and lungs. Additionally, distant recurrences frequently manifest earlier than other subtypes. 180 of the 1601 breast cancer patients investigated by Dent and colleagues had TNBC. In comparison to all other subtypes, they discovered that these women had a higher risk of passing away within 5 years after diagnosis (hazard ratio 3.2; 95% CI, 2.3- 4.5; P.001).They also showed that, in contrast to the other subtypes, where the risk of recurrence was constant, the risk of distant recurrence peaked at about 3 years and then rapidly declined after that. The same team also discovered that women with TNBC were 4 times more likely than women with all other subtypes to develop a visceral metastasis within 5 years of diagnosis.[25] Lin and colleagues discovered that TNBC was linked with worse breast cancer-specific survival (BCSS) and overall survival (OS) compared to HR-positive, HER2-negative tumors (hazard ratio for BCSS 2.99; 95% CI, 2.59-3.45; P.0001; and hazard ratio for OS 2.72; 95% CI, 2.39-3.10; P.0001).In this analysis, TNBC was also linked to a markedly increased risk of death within 2 years of diagnosis, which most likely reflects the propensity of these cancers to manifest distant recurrence within this time frame.[11]

EPIDEMIOLOGY

TNBC disproportionately impacts premenopausal, younger women. Particularly at danger are people with high body mass indices. It is currently unclear how parity, oral contraceptive use, age at menarche, and other common risk factors for the development of breast cancer relate to TNBC.[11] Compared to other breast cancer subtypes, TNBC is diagnosed in African American and women of African origin more commonly. The Carolina Breast Cancer Study discovered that the BL breast cancer subtype had a lower survival time than other subtypes and was more common in premenopausal African American women than postmenopausal African American women and women of other ethnicities of any age. Bauer and colleagues discovered that TNBCs were more frequently found in non-Hispanic black or Hispanic women under the age of 40. They did this using data from the California Cancer Registry. Despite being from a lower socioeconomic class, these women had a worse prognosis compared to those with other breast cancer subtypes, independent of stage.[26] Additionally, numerous studies have demonstrated that TNBC is more frequently seen in patients with BRCA1 mutations. TNBC makes up roughly 60% to 90% of cancers linked to BRCA1 and 16% to 23% of tumors linked to BRCA2. However, BRCA1 or BRCA2 mutations are only present in about 15% of TNBCs.[1]

MOLECULAR CLASSIFICATION AND CLUES TO THE PATHOGENESIS OF TNBC

Microarray-based classification of breast tumors into five intrinsic subtypes—luminal A, luminal B, HER2-enriched, normal breast-like, and basal-like—is the result of the pioneering work by Perou and colleagues. These subtypes are currently recognized by a method known as intrinsic gene or PAM50

subtypes, which was developed as a result of this classification. Although TNBCs were originally thought to be exclusively basal-like breast cancers, it is now acknowledged that TNBCs exhibit a surprising diversity in terms of gene expression. While the majority of TNBCs fall into the basal-like intrinsic subtype on the PAM50 sub typing assay, there is some overlap between the basal-like molecular subtype and the TNBC immunohistochemical subtype.[5] Within the basal-like subtype, further classification of the first classification revealed a claudin-low fraction. These studies raised interesting questions regarding the pathogenesis of TNBCs at the cell of origin and the spectrum of TNBC heterogeneity, even though classifying TNBC into basal and non-basal subtypes was an oversimplification of the TNBC molecular heterogeneity. Lehmann et al. further investigated the heterogeneity of TNBC, finding that there were initially six different subtypes within this group, including basal-like 1 (BL1), basal-like 2 (BL2), immunomodulatory (IM), mesenchymal (M), mesenchymal stem-like (MSL), and luminal androgen receptor (LAR). As they realized that the original transcriptome characteristics of the IM and MSL subtypes were obtained from tumor-infiltrating lymphocytes (TILs) and tumor-associated stromal cells, respectively, they furthered their classification to four tumor-specific subtypes (BL1, BL2,M, and LAR).These four TNBC subtypes each had unique expression patterns, and each subtype differed in terms of immune-modulatory infiltrates. The genes involved in cell cycle, cell division, and DNA damage response (DDR) pathways were enriched in the BL1 subtype. The genetic profile of the BL2 subtype, which included growth factor signalling, glycolysis and gluconeogenesis, and the expression of myoepithelial markers, was distinctive. Cell motility-related gene expression was more prevalent in the M subtype. Despite being ER negative, the LAR subtype was defined by androgen receptor signalling and had gene ontologies that were significantly enriched in hormonally regulated pathways, such as steroid synthesis, porphyrin metabolism, and androgen-estrogen metabolism.[15] Burstein et al. also discovered four distinct subtypes, LAR, mesenchymal (which they refer to as MES), basal-like immune suppressed (BLIS), and basal-like immune activated (BLIS), supporting the idea that four strong subtypes of TNBC can be recognized at the transcriptome level (BLIA). Notably, the disease-free survival rates were highest and poorest for the BLIA and BLIS subtypes, respectively.[16]

CHEMOTHERAPY FOR TRIPLE NEGATIVE BREST CANCER

Historically, compared to other BC types, TNBC had fewer therapy choices. Despite the development of novel biologic and targeted medicines, cytotoxic chemotherapy continues to be the cornerstone of treatment for TNBC. With thorough evidence on the effectiveness of chemotherapy in the neoadjuvant, adjuvant, and metastatic settings, the therapeutic benefits of cytotoxic chemotherapy in TNBC are well established. The use of chemotherapy regimens in the neoadjuvant treatment of TNBC has a significantly greater pathological response rate than hormone receptor-positive (HR+) BC and can dramatically improve the prognosis of TNBC patients. Nevertheless, despite its chemo-sensitivity, TNBC has a generally worse prognosis. Neoadjuvant systemic therapy (NST) is increasingly being used as the standard of care for TNBCs since it has greater pathological complete response (pCR) rates (30–40%) than other BC subtypes. Patients that experience pCR during their initial therapy have better survival results. As a result, pCR is a credible endpoint in clinical trials evaluating the effectiveness of neoadjuvant chemotherapy and is predictive of better long-term results for TNBC. The usual neoadjuvant chemotherapy treatment against TNBC is adriamycin, cyclophosphamide, and paclitaxel, which has pCR rates of 35–45%. Platinum-based chemotherapy has been suggested as a supplement.

Although short-term pCR rates have increased, long-term results are yet uncertain.The National Comprehensive Cancer Network (NCCN) guidelines[11] recommend the following systemic chemotherapy regimens for TNBC: Cyclophosphamide, Methotrexate, and Fluorouracil (CMF), Cyclophosphamide, Epirubicin, Fluorouracil, and Paclitaxel/Docetaxel (CAF), Taxel/Docetaxel, Adriamycin, and Cyclophosphamide (TAC), Adriamycin, and Cyclophosphamide (AC), and Cyclophosphamide, Methotrexate, Flu (CEF-T). Given that BRCA 1/2 proteins are crucial for repairing DNA damage, many DNA damaging agents exhibit enhanced activity in malignancies with germline BRCA mutations.

Preclinical evidence suggests that defects in the BRCA-associated DNA repair process make TNBC tumors more vulnerable to DNA-damaging substances, such as platinum analogues.[23] Because so many of these cancers have BRCA-like characteristics, TNBC is also very sensitive to platinum salts. Conventional chemotherapy regimens were evaluated with and without the addition of carboplatin in two significant randomised trials, the CALGB 40603/Alliance study and GeparSixto, and the results revealed greater pCR rates when the platinum-based drug was used. In 443 patients with stage II and stage III TNBC, the CALGB 40603/Alliance trial evaluated the efficacy of adding bevacizumab +/ - carboplatin to neoadjuvant chemotherapy. With the administration of carboplatin, the percentage of patients who achieved pCR significantly increased from 41% to 54% (OR = 1.71; p = 0.0029). The addition of carboplatin to traditional chemotherapy did not boost long-term OS since the long-term OS was not powered in the experiment.[27] In the GeparSixto trial, Paclitaxel, liposomal Doxorubicin, and Bevacizumab were the mainstays of the treatment regimen for 595 patients with stages II or III TNBC. These patients were randomized to receive either carboplatin or no carboplatin. The pCR rates in the carboplatin group were significantly higher: 53.2% vs. 36.9 (p = 0.005). The addition of platinum to neoadjuvant chemotherapy significantly increased the pCR rate from 37.0% to 52.1%, according to the findings of a meta-analysis that examined nine randomized controlled trials (RCTs) (n = 2109) (OR 1.96, 95% confidence interval (CI) 1.46-2.62, p 0.001). In the BrighTNess experiment, a randomized phase III clinical trial with three therapy arms and a total of 634 TNBC patients, Loibl et al. published their updates: Paclitaxel alone (P) (n = 158), Paclitaxel plus carboplatin alone (PCb) (n = 160), and Paclitaxel, carboplatin, and the PPAR inhibitor Veliparib (PCbV) (n = 316) make up the standard neoadjuvant regimen. With a 4-year follow-up period, event-free survival, OS, and safety outcomes were evaluated. When carboplatin was added to paclitaxel-based neoadjuvant treatment, either with or without the addition of veliparib, pCR was markedly improved. Additionally, the addition of carboplatin to paclitaxel increased the pCR and EFS without raising the risk of acute myeloid leukaemia or myelodysplastic syndrome. EFS with PCbV had an HR of 0.63 (95% CI: 0.43-0.92, p = 0.016) and EFS with PCb had an HR of 0.57 (95% CI: 0.36-0.91, p = 0.018) when compared to P alone.[28] According to the most recent American Society of Oncology (ASCO) guidelines, individuals with TNBC may be given carboplatin to enhance pathologic complete response.[17] Clinical trials are still being conducted to examine the impact of platinum drugs in patients with TNBCs that are both BRCA-mutated and non-BRCA-mutated (NCT02413320 and NCT02547987).[14]

ADJUVANT VERSUS NEOADJUVANT CHEMOTHERAPY

TNBC has a poor prognosis, however research has shown that it responds to treatment better than other molecular subtypes. Third-generation chemotherapy is advised according to both NCCN and the

European Society for Medical Oncology (ESMO) guidelines since conventional therapies for patients with HR-positive and/or HER2-positive breast tumors are ineffective in TNBC. Adjuvant (after surgery) and neoadjuvant (before surgery) administration of the same chemotherapy treatment results in equivalent disease-free survival (DFS) and overall survival (OS), according to a number of sizable randomized clinical trials.7 There was no survival benefit for receiving doxorubicin and cyclophosphamide in the neoadjuvant setting compared to the adjuvant setting in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-18 trial. When preoperative docetaxel was added to AC, the number of pathologic complete responses (pCRs) increased significantly (26% vs 13%; P.0001), but there was no significant difference in DFS or OS, according to NSABP B-27's comparison of AC with preoperative or postoperative docetaxel. Women with breast cancer undergoing adjuvant versus neoadjuvant chemotherapy showed no difference in OS, disease progression, or distant recurrence, according to a meta-analysis of 9 randomized clinical studies. These studies proved the effectiveness of anthracycline- and taxane-based regimens, and they served as the foundation for more recent clinical trials, notably those that involved TNBC patients receiving neoadjuvant therapy. While some individual trials' subgroup analyses revealed conflicting outcomes for anthracycline-based therapy in TNBC subpopulations, the majority of studies—including a meta-analysis of five randomized clinical trials—indicate a positive effect in TNBC. Results of numerous subgroup analyses of significant phase III adjuvant trials support the use of taxanes as adjuvant therapy for TNBC.[12]

NEOADJUVANT CHEMOTHERAPY

For individuals with earlier stages of operable breast cancer, neoadjuvant chemotherapy is now often administered. Neoadjuvant chemotherapy is currently utilized to downstage big tumors so that breast conserving therapy can be employed for locally advanced breast cancer, inflammatory breast cancer, and other types of breast cancer. Clinically node negative breast cancer patients with unfavourable tumor characteristics, in whom adjuvant systemic therapy is anticipated, are now included in the indication for neoadjuvant chemotherapy.[8]

PREDICTORS OF RESPONSE TO NEOADJUVANT CHEMOTHERAPY

The difference in tumor size between pretreatment clinical and/or radiologic measurement and posttreatment status is used to assess the response of neoadjuvant chemotherapy. Neoadjuvant chemotherapy can result in a range of responses, including total response, partial response, and non-response. Both axillary lymph nodes and breast cancers share this idea. According to studies, the rate of therapeutic response varies from 15% to 30% depending on the kind of tumour and the chemotherapy regimen used. When compared to patients whose tumors do not react to treatment, those who complete a complete response to neoadjuvant chemotherapy have superior results, including longer periods of time without developing a disease and longer overall survival. Complete pathologic response has not been consistently defined as a surrogate criterion that predicts long-term clinical benefit. The three definitions that are most frequently used are: absence of invasive cancer and in situ cancer in the breast, axillary lymph nodes, and ypTO/is ypNO; absence of invasive cancer in the breast regardless of ypTO/is ypNO; and absence of invasive cancer in the breast regardless of ypTO/is ypNO; and absence of invasive cancer in the breast regardless of ypTO/is ypNO; Cortazar et al.[22] investigated the association between pathological full response and patient outcome using data from 12 recognized international trials with

11,955 individuals. The goal was to define pathological full response and to pinpoint the subgroups of breast cancer that were thought to respond best to neoadjuvant chemotherapy. According to the authors of this data, patients who demonstrated a pathologic complete response—defined as ypTO ypNO or ypTO/is ypNO—had a greater chance of surviving.[19] This effect was particularly obvious in tumor subtypes that were more aggressive, such as triple-negative breast cancer and tumors that were HER2-positive and hormone receptor negative. They suggested a stricter definition, namely pathological full response. As previously stated, survival was unaffected by the presence or absence of ductal carcinoma in situ in individuals with absolutely no evidence of invasive cancer in the breast and lymph nodes. A German pooled analysis of seven neoadjuvant studies casts doubt on this conclusion because it revealed that individuals without ductal carcinoma in situ have a better prognosis than those with residual ductal carcinoma in situ but no residual invasive carcinoma in the breast. The presence of tumor-associated lymphocytes, tumor necrosis, high tumor grade, high tumor grade, and tumor size are all thought to be indicators of a greater response to neoadjuvant chemotherapy. Additionally, patients with triple-negative breast cancer, HER2/neu oncogene positive tumors, and hormone receptor negative tumors respond to therapy better.[18]

PREDICTORS OF NON- RESPONSE TO NEOADJUVANT CHEMOTHERAPY

Additionally, partial or no response to therapy can be predicted by gene expression analysis, allowing for the avoidance of needless chemotherapy. Molecular subtyping may help identify patients who might not benefit from neoadjuvant chemotherapy, according to recent research employing BluePrint and MammaPrint. The luminal group can be divided into luminal A and luminal B kinds thanks to gene profiling. Neoadjuvant chemotherapy does not improve the prognosis for cancers of the luminal A type.[21] However, therapy for luminal B cancers frequently proves difficult. They are typically treated with both hormone treatment and chemotherapy, frequently without success because they are more aggressive than luminal A kinds. It is possible to design a more efficient endocrine therapy when it is known that luminal B/HER2 tumours do not react to chemotherapy.[18] Balmativola et al. in 2014 described their experience among a cohort of 490 cases displaying pathological complete response and partial response compared with the group of non-responders in order to identify these patients who will not benefit from neoadjuvant chemotherapy. They supported previous research's findings that oestrogen and progesterone positive was linked to a worse prognosis after neoadjuvant treatment. In addition, they showed that patients who did not respond to neoadjuvant chemotherapy were more likely to have the lobular subtype of breast cancer and to lack tumor-infiltrating lymphocytes. The expression of oestrogen or progesterone receptors, however, was found to be an independent variable for separating the no response category from those who had complete and partial responses when utilizing multivariable analysis. This finding may confirm the hypothesis put out by Delpich et al. that no neoadjuvant chemotherapy response may be more closely associated with intrinsic tumor features than oestrogen receptor expression.[20]

BENEFITS OF NEOADJUVANT CHEMOTHERAPY

It provides a rare opportunity to assess therapy response, with complete pathologic response serving as a stand-in for a survival endpoint, and to more quickly determine the efficacy of new therapeutic drugs and to stop ineffective treatment earlier. Additionally, changing the dose and/or switching to a different

medicine in the event of therapy resistance spares patients from the burden of toxicity and side effects. Neoadjuvant chemotherapy also offers the chance for personalized treatment and permits the collection of tumor samples before, during, and after therapy for translational research. This analysis of the behavior of the tumor while it was being treated in situ with neoadjuvant chemotherapy and its link with the clinical outcome is a great model to ascertain the prognostic significance of tumor characteristics. The development of specially designed treatment plans based on unique risk profiles is the ultimate objective of translational research related to neoadjuvant chemotherapy.[18]

SURGICAL OUTCOMES

Neoadjuvant chemotherapy enables tumor volume decrease in the original tumor and the nearby nodes, which may open up more surgical treatment options. Numerous studies have shown that neoadjuvant chemotherapy helps shrink tumors, enabling higher rates of BCS. Lumpectomy was performed more frequently in the preoperative chemotherapy group than in the postoperative group (67% vs 60%; P.002) in the NSABP B-18 trial, where patients were assigned to preoperative vs postoperative chemotherapy. BCS was compared to complete mastectomy without radiation in a retrospective study of 1242 individuals with pathologic T1-2N0 TNBC treated at the Memorial Sloan Kettering Cancer Center. There was no discernible difference between the 2 groups in terms of local recurrence, distant metastasis, total recurrence, DFS, or OS.[29] Since the NSABP studies shown that there is no difference in survival based on the date of chemotherapy delivery, it may be assumed that identical results would be seen in the neoadjuvant group even though none of these patients received neoadjuvant chemotherapy.

PATHOLOGIC RESPONSE TO CHEMOTHERAPY

After neoadjuvant therapy, pCR is defined as the absence of residual invasive cancer on pathologic assessment of the resected breast main and local lymph nodes. Numerous neoadjuvant studies have demonstrated that pCR is a promising surrogate metric for DFS and OS because it predicts long-term results. In comparison to luminal tumors, highly proliferating carcinomas such TNBC or HER2-positive tumours are more likely to achieve a pCR. Patients who achieved a pCR had longer event-free survival (EFS) and overall survival (OS), according to a significant pooled analysis of 12 randomized clinical trials of neoadjuvant chemotherapy in breast cancer conducted by the Collaborative Trials in Neoadjuvant Breast Cancer international working group.[1] The highest correlation between pCR and long-term outcomes was observed in trastuzumab-treated patients with TNBC and HER2-positive, HR-negative malignancies. Results for patients with stages I to III breast cancer who underwent neoadjuvant chemotherapy were reported by Liedtke and colleagues from the MD Anderson Cancer Center.[13]

CONCLUSION

Treatment advancement for TNBC is still a significant challenge. Systemic chemotherapy is necessary for the majority of patients because of the aggressive biology and high risk of distant recurrence. Patients with locally advanced illness benefit from neoadjuvant chemotherapy because it shrinks the tumor and increases the likelihood of BCS. Neoadjuvant treatment is an appealing option for all patients with TNBC because clinical and pathologic responses offer crucial prognostic information. The enhancement of pCR rates and outcomes for patients with residual disease are the main topics of clinical

research in the neoadjuvant context. The development of new targeted therapies and immunotherapeutic medications is ongoing. Due to the significance of variation in TNBC subtypes, it is challenging to carry out more focused investigations. All TNBC patients who are thought to be candidates for systemic chemotherapy should be given consideration for treatment in the neoadjuvant setting given the benefits neoadjuvant therapy provides.[1] The effectiveness of neoadjuvant carboplatin with docetaxel in TNBC is favourable. Patients who complete this treatment and achieve pCR or RCB I show excellent 3-year RFS and OS without adjuvant anthracycline.[2] Neoadjuvant chemotherapy is currently a very popular kind of treatment for breast cancer. Pathologists, radiologists, surgeons, and oncologists must work together in a well-established integrated multidisciplinary care model to assess the response to neoadjuvant chemotherapy. Prior to neoadjuvant chemotherapy, access to diagnostic and prognostic/predictive data of breast tumors and sentinel lymph nodes is crucial for providing an accurate reporting of the pathologic response to therapy. A pathologist's duties include handling and processing post-treatment surgical specimens correctly, including identifying the tumor bed for determining the therapy response, thoroughly sampling the tumor bed, measuring the size of the residual tumor, and figuring out the extent of the residual tumor, its cellularity, and the treatment's effects in both the breast and lymph nodes. To determine whether a residual tumor is present or not, immunostains for macrophage and epithelial markers may be employed. The level of response to neoadjuvant chemotherapy may be graded using Ki-67. Neoadjuvant chemotherapy may cause the hormone receptors HER2/neu oncogene to alter in status. Respecting the specified rules will ensure correct reporting of neoadjuvant chemotherapy's effects and proper management of breast cancer patients.[18] Neoadjuvant therapy for early stage TNBC has recently advanced. For the right subtypes of TNBC, ICI plus PARPi may become the standard of therapy. In the treatment of HRD tumors or BRCA-associated malignancies, carboplatin is still crucial. Testing innovative targeted therapy in the neoadjuvant environment may be greatly facilitated by novel clinical trial designs like I-SPY 2 or ARTEMIS.[24]

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