Review on Assessment of Response of Neo-Adjuvant Chemotherapy in Patients of Carcinoma Breast by High Frequency Ultrasound

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ABSTRACT

Neo-Adjuvant Chemotherapy (NACT) is used in patients with breast cancer to reduce tumour focus, metastatic risk, and patient mortality. Neoadjuvant treatment of breast cancer has become established as a safe and often effective therapeutic approach of choice for larger primary and for locally advanced breast cancer. Neoadjuvant approach offers the advantages of down staging the disease, potentially reducing the extent of surgery and in an era of individualisation of therapy, tests the efficacy of therapy administered to patients. The preoperative setting is also an effective way to study the activity of novel agents or therapeutic combinations in vivo against human breast cancer. For new therapies, preoperative trials avoid the issue of adaptive resistance and pre-treatments that can be problematic in the advanced disease setting. Monitoring NAC effects is necessary to capture resistant patients and stop or change treatment. The existing methods for evaluating NAC results have some limitations. Quantitative ultrasound information can characterise the tumour's pathological response better and at an earlier stage of therapy than the assessment of the reduction of its dimensions. The introduction of statistical parameters of ultrasonic backscatter to monitor the effects of chemotherapy can increase the effectiveness of monitoring and contribute to a better personalisation of NAC therapy.

KEY WORDS

Carcinoma Breast, Locally Advanced Breast Cancer, Neoadjuvant Chemotherapy, Anterior Chemotherapy, High Frequency Ultrasound, Ultrasonography.

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BACKGROUND

Carcinomatous condition is characterised by division of cells, which is not controlled and is aberrant.¹ Risk factors of cancer are associated with ecological variables, lifestyle characteristics and genetic composition.² The impact of it posed in society can be quantified by assessing its negative outcome on community health, quality of life and its cost implications to the health care delivery system.³ Great efforts are made to improvise the diagnostic and therapeutic aspect for cancer associated morbidity and mortality outcomes. Hence, the research is now focussed on the onset of its symptoms, natural history and apt therapy for cancer, involving normal cell transformation into cells exhibiting rapid and unstable cell division.⁴ Various factors influence tumourigenesis like oncogenes overexpressed, amplification of cell signal and angiogenesis.⁵

Notably, factors remain dependant for growth of tumour, as in case of, oncogenes like ras / MAP kinase which demonstrate initiation of neo blood vessels in tumours, promotion of tumour growth rate, enhancement of cell signalling activity and increase in the ability to invade and metastasise. On the contrary, various genes perform in tumour growth suppression (such as tumour suppressor genes) and also participate in the DNA repair procedure; for instance, BRCA1 and BRCA2 genes.⁶ Hanahan and Weinberg defined tumourigenesis and listed 6 principle and interacting cancer characteristics.⁷ These involve -

1. Tumour cell immortality via deregulated cell senescence.
2. Resistance factors to cell morbidity.
3. Signalling defects promoting tumour cell multiplication.
4. Blockage of growth suppressors.
5. Rise in angiogenesis.
6. Establishment mechanisms for invading and metastasising.

Carcinomatous cells are usually programmed to remain "immortal" and progresses to multiply in uncontrollable manner, in comparison to the healthy cells which either are dead or infused to senescence situation. Other actions include defects in cell signalling pathways inhibiting apoptosis,⁸ which is controlled by anti-apoptotic amino acids, including surviving, caspase, Bcl-2, and p53.⁸ A significant part of metastasis includes angiogenesis and neovascularisation.

Exceeding a growth of 2 mm,³ tumours necessitates a blood supply to providing nutrition, oxygen and transportation of blood-borne biochemical signals for survival. The growing blood supply is even controlled by tumour cells which releases proangiogenic factors like VEG-F (Vascular Endothelial Growth Factor), angiogenin, angiostatin, and transforming growth factor. Tumour cells also down-regulate angiogenesis inhibitors such as angiopoietin-2, angiotensin, and angiostatin-2 leading to uncontrollable vascular growth.⁹ Tumour vasculature even enhances spread of cancer cells risk, as vascular supply serving as pathways for circulation of tumour cells.⁷ Breast Cancer (BC) is a leading oncologic disease of active working age, being also the main malignant tumour mortality cause among women. It forms the first frequented cancer form in women, followed by skin cancers of non-melanoma forming type.¹⁰ The need of neoadjuvant chemotherapy is required so as to portray a significant role in down staging the tumour. Hence, in the current review, we summarise latest literature throwing light

on the neoadjuvant chemotherapy response in carcinoma breast patients by high frequency ultrasound. In the next segments, we provide a view of historical information that is based on existing therapeutic and research interventions.

EPIDEMIOLOGY-INCIDENCE AND MORTALITY

Worldwide, carcinoma of the breast ranks as the second highest diagnosed type. Occurrence varies across geographic location; with incidence rate of 27 for every 100000 African and Asian population, which increases to 96 for every 100000 European individuals and 92 for every 100000 North American population. When mortality rates are considered, cancer of the breast ranks as 5th largest cancerous lesion resulting in death when compared to other malignant lesions. Every year, 52000 individuals succumb to breast cancer.¹⁰ Death rate varies significantly between developing and developed nations, which could be attributed to variations in health care setup, capability in availing early diagnosis and therapy.

The World Health Organization (WHO) statistics demonstrated 8.2 million casualties due to cancer worldwide.¹⁰ International Agency for Research on Cancer (IARC) report of 2012 year, the overall world cancer burden is about 14.1 million new cases and expected to increase to 19.3 million by 2025 above the age of 15 years. Breast cancer patients are highest amongst all the cancer in both the sexes' world-wide.¹¹ There is a higher burden of breast cancer in both developed and also the developing countries with very high death rate in developing countries amongst the younger patients i.e. 67.8 / 1000. Average in the age group of 15 - 49 years is 94 deaths per thousand and about 331 deaths above 50 years. Diagnosis in early stages of breast cancer and 5 years survival is 90 % in the US whereas 76 % of patients in India have advanced stage disease at presentation.¹²

Late medical help may be because of ignorance of the disease, painless nature, and fear of losing the breast, economical constraints or lack of access to medical facilities. ICMR estimated 144000 new breast cancer patients in India and metro cities like Mumbai, Bangalore have reported higher incidence of this disease.¹³

We conducted a systematic search of PubMed for key words in systematic strategy (locally advanced carcinoma breast) or (carcinoma breast locally advanced) or (operable carcinoma breast) or (breast cancer) and [filter] and (ultrasound) or (ultrasonography) or (high frequency ultrasound) or (USG) and (neoadjuvant chemotherapy) or (preoperative chemotherapy) or (systemic neoadjuvant chemotherapy) with inception dates to March 2020, and picked all relevant studies, without any restriction to any language. Reference lists of articles with full text were searched and analysed literature from every relevant article to identification of omitted literature.

RESEARCH QUESTION

The purpose of this study was to recognise the widely used imaging system to assess the outcome of neoadjuvant chemotherapy in cases of regionally advancing breast cancer.

NATURAL HISTORY AND PRESENTATION

Natural progression of breast carcinoma with epithelial cellular transformation of end duct lobules units (TDLU).¹⁴ During diagnosis, cancer of breasts might be categorised as into non-invasive (in situ) or invasive type of breast cancer. Breast cancer of non-invasive is a characteristic of tumours limited to mammary duct lumens.¹⁵ An illustration of non-invasive type of breast carcinoma is Ductal Carcinoma In Situ (DCIS), accounting to approx. 20 percent of incident breast cancer cases,¹⁴ DCIS and LCIS (Lobular carcinoma in situ) both are considered as precursors to invasion type breast cancer and its nomenclature referring to their closeness to the mammary ducts (DCIS), or terminal duct lobular units (LCIS).¹⁶

Disease in situ (A) is identified as pathologies limited to ductal area itself, like ductal carcinoma in situ. B. Invasive carcinomas represent features depicting degrading of the basement membrane (myoepithelium) and invading to the proximal breast parenchyma. Lesions spreading further from

the lumen of breast ducts and traversing into approximating parenchyma is termed as invasive carcinoma. 17 different subtypes are identified, that is characteristic of differing histological and molecular characteristics like hormone receptor status, growth hormone amplification, or tumour cell type.¹⁷ In addition, as breast cancer invades, it is classified into levels based on tumour size, lymphatic spread and into other body parts.

RISK FACTORS FOR DEVELOPING BREAST CANCER

- Race**
 Newman in 2009 conducted a study in which by chance, Stage 3 breast carcinoma (i.e., regionally advanced) was suggested as greatest (16.6 %) in Black coloured females in all ethnic groups. On comparing, Asiatic females showed least breast cancer occurrence.¹⁸
- Gender**
 Leone et al in 2015 stated that sex proves to be a prominent risk factor for incident cases; gender poses as an eminent risk variable for incidence; presence of breast cancer in males is scarce accounting to 1 % of cases.¹⁹ Meanwhile, Siegel et al in 2015 stated that 10 years later, occurrence rates have raised to 2350 diagnoses in 2015 with a stabilised death rate of 440 deaths (18.7 %) annually in the United States of America.²⁰
- Age**
 Siegel et al stated that possibility of breast cancer occurring is at 12.3 % in lifetime with an increased risk with advancing age. 60 years is the median age for

development of breast cancer. Peak occurrence reported is at 70 years in women, with women demonstrating 6.7 % probability in this age group.²⁰

4. **Family History and Genetic Conditions**

Lichtenstein et al in 2000 stated that the hereditary factors make up to 27 percent of risk for breast cancer.²¹

5. **Gynaecological and Obstetric History**

McPherson et al in 2000 concluded that the reproductive variables are related to risk of breast cancer which included menarche age, menopausal age, parity. Female reaching menarche during earlier years of adolescence pose a higher risk for developing breast cancer.²²

6. **Lifestyle Factors**

McPherson et al also stated that the individual's lifestyle experience might render significant data material for risk factors including diet, and weight. Poor diet elucidates high fat consumption, and obesity is thought of as risk factors for breast cancer, with the risk doubling in case of patients who are obese. Also, consumption of alcohol and smoking are also associated with increased risk to develop breast cancer in a lifetime.²²

SCREENING AND DIAGNOSIS

Breast cancer screening is performed in either of 2 paths:

1. Self-Breast Examination (SBE).
2. Routine or immediate referral from the General Practitioner (GP).

The practice and education of SBEs do not reduce mortality, but increases awareness which forms a significant point in breast cancer screening.²³ Screening includes

1. Clinical evaluation
2. Mammography and / or ultrasound evaluation
3. A Fine Needle Aspiration (FNA) or core biopsy for histological assessment

Thomas et al conducted a prospective study to examine 266064 Chinese females above 10 – 11 years. Patients were randomly recruited into two groups receiving either instructions for SBE or those who didn't receive any training for SBE. Findings of the study demonstrated similar mortality rates associated with breast carcinoma amongst categories (taught category, n = 135 versus non-taught category, n = 131).²³

Magnetic Resonance Imaging (MRI) might be suggested for individuals in case of poor quality of mammography or to evaluate the size of tumour in case of breast conservation surgery indication. Methods of structural imaging [ultrasound investigation (USI), x-ray mammography, magnetic resonance imaging (MRI)] that allow detecting dimensional changes of the lesion are not suitable for early assessment of the tumour response to the administered therapy.²⁴

Imaging modality has a significant part in detecting benign and malignant masses in the breast. Miller et al conducted a study to compare survival data amongst 89835 women randomly divided into two categories; yearly physical / clinical evaluation utilising mammography against a control group (without mammography and only physical examination). 1.05 hazard score was reported amongst the

two patient categories. The study was of the conclusion that the survival benefit was nil with regular mammography conducted in women on yearly basis.²⁵

Hormone receptor literature like Oestrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal growth factor Receptor-2 (HER2 / neu) are regularly performed in carcinoma of breast which facilitates both tumour prognosis and treatment decision. The aim of performing receptor status is providing correct therapy to the correct patient. The pathologist's role is to assess the biomarkers accurately, and oncologist's role is to intervene patients with either of the varied on hormonal status.²⁶ Hormone receptors such as ER and PR seen on the breast cells results in cell growth after picking up hormonal signals. The presence of hormonal oestrogen receptors makes it ER-positive (ER +) receiving signals from oestrogen and promoting growth, similar to normal cells. Likewise, the presence of hormonal progesterone receptors makes cancer PR positive (PR +). So, this makes that cancer cells receiving signals from progestogens might promote its growth. In the same way, HER2 / neu positive (HER2 / neu +) status of the breast carcinoma meant that HER2 / neu gene is producing too many HER2 / neu proteins. HER2 / neu proteins are receptors found on breast cells. Usually, HER2 / neu receptors regulate healthy breast cell development, multiplication and repair. But still, HER2 / neu gene will fail to work properly in 30 % cases of breast cancers making many copies referred to as HER2 / neugene amplification.

The excess HER2 / neugene copies instructs breast cells to produce lots of HER2 / neu receptors (HER2 / neu protein overexpression). This finally results in growth of breast cells and multiply in an uncontrollable fashion. Biomarkers might be either prognostic or predictive or both. Biomarkers of prognostic type quantify prognosis not dependent on any other factors. Mortality or recurrence of disease is directly correlated with the biomarkers. Meanwhile, predictive biomarkers suggest the responsiveness of patients to provided intervention. The hormonal receptors presence (i.e. ER, PR) in breast cancer cases is an illustration of meek prognostic, yet stronger predictive marker. In case the tumour expresses the receptors; they can then measure the benefit of endocrinal therapy (tamoxifen). Oncogene HER 2 / neu when over expressed in host makes an illustration for both prognosis and prediction biomarkers. Expression of HER2 / neu is correlated compromised prognosis (greater risk of recurrence [ROR]); But still it even predilects that an individual might be greatly benefitting from anthracycline and taxane-based chemotherapeutic intervention and treatments targeting HER2 / neu (trastuzumab) but fail the endocrine dependent intervention.²⁶

There are different methods to assess axillary lymph nodes. 1) Physical examination by physician- 25 - 32.3 % sensitivity with very low specificity, 2) Magnetic resonance imaging has sensitivity 36 - 78 % and specificity 93 - 100 %, 3) There is technical difficulty in imaging the axillary lymph nodes in mammography, but if lymph nodes are detected it's specificity is 99.5 % for identification of metastasis. Ultrasonography which is easily available tool has 45.2 - 86.2 % sensitivity and 40.5 % - 86.6 % specificity.²⁷

An ultrasonographic feature of breast cancer varies as per the hormonal behaviour of the tumour i.e., triple negative breast cancers²⁸ and HER over-expression.²⁹ Bedi et al

suggested six different morphological features of the lymph nodes categorising those to suspicious of metastatic, indeterminate or benign lymph nodes.³⁰

Maximum cortical thickening has a positive metastatic association more with histopathology than cytology, where as other imaging features like size and contour, cortical morphology and hilar fat failed to predict its correlation in patients with clinically node negative axilla.³¹

Enlarged lymph nodes of 5 mm diameter showed the 87 % sensitivity and 56 % specificity, isolated size has poor sensitivity for metastasis. In the advanced stage of metastatic burden in the lymph node there is rounding and loss of fatty hilum, these features on ultrasound are highly specific for metastasis. Additional use of colour Doppler / power Doppler or elastography or use of contrast media increases sensitivity 83.33 % specificity 84.38 % but it is not recommended for routine use by European society. Updated guidelines of American Society of Clinical Oncology 2014 and European Society for Medical Oncology 2015, it is emphasised that clinical evaluation should be assisted by ultrasound (US) of axilla and if a suspicious lymph node is identified, FNAC or FNAB (Fine Needle Aspiration Biopsy) from a particular site of suspicion. (Evidence IIIA) SLNB (Sentinel Lymph Node Biopsy) was considered to be standard of care in N0 axilla.³²

Lee et al have demonstrated that abnormal lymph nodes with larger tumours had higher rates of metastasis and ultimately recommended its use in tumour stage T1C. It also does not delay the initiation of the definitive therapy. Sonologically positive axilla in NACT (Neo-Adjuvant Chemotherapy) patients should be considered for axillary lymph node detection.³³

There is a different response to chemotherapy depending on the immunological subtypes of breast malignancy. Mammography and USG showed better correlation with pCR (Pathologic Complete Response), i.e. sensitivity 78.6 % and specificity 92.5 %. It is observed that micro metastasis present in early stages and larger tumour are prone to develop resistance to chemotherapeutic agents. Outcome of NACT will depend on size and cellularity of primary tumours and size and number of the lymph nodes. Extent of residual tumour has significant impact on distant relapse. pCR of primary tumour has lower rates of negative residual metastasis. Prognosis in the NACT patient will depend on response to chemotherapy and biological markers of the tumour which are not a part of traditional staging of breast cancer.³⁴

Different pathological responses are observed to anthracycline based chemotherapy regime and taxane based regimes. Thirty percent total pathological response (pCR) with anthracycline based chemotherapy and 40 % with taxane based chemotherapeutic agents in triple negative tumours was observed in breast cancer patients, addition of immunotherapeutic agents to chemotherapy in HER-2 positive tumours increased response to 70 %.³⁵

Ki-67 IN BREAST CANCER

Ki-67 protein in human beings is coded by MK167 gene and is a cellular marker for multiplication, which is a nuclear protein and is put forth as proliferating cells yet is not seen in resting cells. The Ki-67 expression as identified by immunohistochemistry is one of the greatly consistent

indicators of the proliferative status of cancer cells. The major significant characteristics defining the therapy and outcome in breast cancer are ER, PR, and HER2 / neu status though few authors report Ki-67 in addition to ER, PR, and HER2 / neu. The current guidelines of the American Society of Clinical Oncology does not include Ki-67 in the enlisted required routine biological markers. Yet, the discovery of neo-genetic tests has stressed the part of proliferative genes, including Ki-67, as prognostic and predictive markers.³⁶ The most generally utilise way to detect Ki-67 positivity is by staining with the MIB-1 antibody. The Ki-67 score is defined as the percentage of total number of tumour cells with nuclear staining, while rest measure many hundred nuclei in various arenas of tumours to provide a total average index. This can be attributed for the adequate inter laboratory and intraobserver variability. A standardisation of Ki-67 pathological evaluation isn't still accomplished.³⁷ This deprivation of consistency across laboratories has constrained the participation of Ki-67, till the time, it will be adequately standardised. Soliman NA, Yussif SM did a study in 2016 to assess the practical importance of Ki-67 index as a prognostic marker and predictor of recurrence in various molecular subcategories of breast cancer among 107 cases of primary breast cancer. Cases with Ki-67 lesser than 15 % showed greater overall survival than those with Ki-67 greater than 15 %. Cases with Ki-67 greater than 15 % demonstrated higher incidence of metastasis and recurrence when compared to Ki-67 less than 15 %.³⁸

LOCALLY ADVANCED BREAST CANCER AND TREATMENT

Locally advanced breast cancer, described at third stage of pathology, is a lesion which is bigger than 5 cm involving lymphatics, skin and chest wall.¹⁸ Locally advanced breast cancer needs multimodality intervention to solve both local (primary) disease and possible distant microscopic metastasis. Pre-operative (neoadjuvant) chemotherapy for LABC (Locally Advanced Breast Cancer) (stage 3 disease) might possess important practical and clinical benefits.³⁹ Neoadjuvant chemotherapy (adjuvant / basal / induction / primary / preoperative chemotherapy) is administered preoperatively in LABCs for reducing tumour size and a better surgical approximation.

The benefits included down-staging inoperable breast tumours to help resection and letting doctors to evaluate tumour response during therapy. The role of imaging for patients treated with neoadjuvant intervention for breast cancer is not just to evaluate the therapeutic response measured as tumour shrinkage, but even in prediction of histological response to chemotherapy, that is associated with survival. Latest clinical studies done in with breast cancer cases have demonstrated that therapy with chemotherapy prior to definitive surgery (neoadjuvant) leads in equal survival overall when compared with a surgery-first treatment plan. By decreasing tumour bulk prior to definitive surgery, neoadjuvant chemotherapy gives an opportunity for breast conservation and for a smaller excision size.^{40,41}

Neoadjuvant chemotherapy was utilised initially in locally advanced breast cancer and inflammatory cancer situations.⁴² Neoadjuvant chemotherapy decreases metastasis and micro-metastases risk in distant cell structures. It even decreases the

neoplastic foci and also the recurrent rates and death rates of affected individuals. Neoadjuvant chemotherapy is generally utilised for treatment of locally advanced carcinoma, yet present trend is to include the usage of neoadjuvant therapy to T1 tumours. Additionally, neoadjuvant therapy renders better opportunities for response prediction 1 and comparatively fast evaluation for drug development and approval in breast cancer 2 by assessing success rate from the therapy at early stages of disorder.^{43,44}

Neoadjuvant Chemotherapy in Breast Cancer

Neoadjuvant chemotherapy is marked in downstaging bigger or regionally advancing lesions that allows for breast-conservation operations, hence preventing mastectomy, employed in the early 1970s. Cases achieving a complete pathological response to neoadjuvant chemotherapy has demonstrated lesser recurrence rates on comparison to those having partial response. But still, pCR is attained in only 20 to 30 percent of cases, and tumour biology is dependent on their predictive value. Cases presenting human epidermal growth factor receptor 2-positive and triple-negative tumours are strong contenders for neoadjuvant chemotherapy because of their increased possibility of obtaining pCR.

Residual Cancer Burden (RCB) combining pathologic quantifications of size and cell structure of primary tumour and frequency and size of lymphatic metastases gives a standardised method for the prospective assessment of specimens to measure neoadjuvant chemotherapy's response. RCB is demonstrated to have prognostic value for long-term survival post neoadjuvant chemotherapy in all 3 subsets of breast cancer, oestrogen receptor alpha positive (ER+), HER2-negative, and triple-negative disease.⁴⁵⁻⁴⁹ Falou O et al in their study (2013) investigated the possibility of ultrasound elastography for evaluating therapy responsiveness for locally advancing breast carcinoma in 15 females who received neoadjuvant chemotherapy. Strain ratio utilising static ROIs were seen to be the apt predictor of treatment response, with 100 percent sensitivity and 100 percent specificity attained 4 weeks after the intervention.⁵⁰

Effects on Nodal Disease

The level of axillary node being involved consequent to neoadjuvant chemotherapy forms the greatest predictor of consequent relapse. Therefore, individuals placed under neoadjuvant therapy possess, conventionally, progressed to axillary clearance during the period of breast removal or conservation. Yet, biopsy of sentinel lymph node remains the choice of axillary therapy in breast cancer operation and about 40 percent of axillae might transform from disease present to exhibit a wholly pathological documented response subsequent to neoadjuvant therapy. Suspicious axillary nodes visualised on diagnostic imaging must be biopsied by fine-needle aspiration or core-needle biopsy to prove metastatic entanglement; Yet a negative biopsy or the inconspicuousness of suspicious nodes on ultrasound will not exclude axillary metastasis. Sentinel lymph node biopsy must be planned during definitive surgical resection of the primary tumour in cases with a 'negative' axillary work-up on the original,

prechemotherapy axillary evaluation. Few have suggested a sentinel lymph node biopsy be performed prior to administering neoadjuvant intervention; But still, this method remains controversial as clearance of involved axillary nodes with neoadjuvant intervention is a better prognostic indicator than response in the primary breast tumour alone and removing sentinel node which will not let for total assessment of pathologic response in the axilla. Also, perhaps more logically, advocate sentinel node biopsy after chemotherapy, mentioning the decreased necessity for axillary lymph node dissection for node-negative cases.⁵¹⁻⁵³

Measurement of Response

Conventionally, responsiveness to neoadjuvant therapy, preferentially aided by mammographic evaluation, was determined as a measure of the effectiveness of intervention, specifically in the beginning of endocrine intervention for older females. Advancements in ultrasonography, magnetic resonance imaging and in the recent times functional imaging with MRI and positron emission tomography / computed tomography represents which in present day's practice and clinical studies, ultrasonography and MRI are usually considered needed to substantially evaluate neoadjuvant tumour responses. Yet, mammography might be utilised to measure the tumour's endocrine therapy responsiveness in older age females provided the (usual) lucency of the adjacent healthy breast mass. But still, ultrasonography carries the advantage of comfort and simplicity, considering that patients have to make multiple visits and thus obtaining a 3 D dimensional imaging of reproducible type for quantifying and recording tumour response that is not involving radiation or specifically complex instrument. During and subsequent to neoadjuvant chemotherapy, MRI might be the finest imaging modality available to evaluate the disease extent and the possible success of breast-conservation operation. There are issues related radiological imaging and histopathological evaluation as well tumour behavior. Hence, the present study is done to assess neoadjuvant chemotherapy response in carcinoma breast patients by high frequency ultrasound.⁵⁴

CONCLUSIONS

Neoadjuvant therapy remains an indispensable tool exhibiting great potential in advanced breast cancer therapies. In clinical practice, neoadjuvant therapy is usually applied for 90 days to ascertain a particular tumour volume reduction response allowing breast-conservation surgery. Hence, establishing molecular variation in the early weeks of neoadjuvant intervention might facilitate in identifying potential biomarkers of response. Overall, the neoadjuvant setting is an assuring technique for faster induction of efficient and personalised newer interventions and also as biomarkers for precision oncology to obtain therapies for breast cancer into the clinical perspective.

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