Central Asian Journal of Medical and Pharmaceutical Sciences Innovation **1**(2): 81-96 (2021)

RESEARCH PAPER

Triple-negative breast cancer: biology, pathology, and treatment

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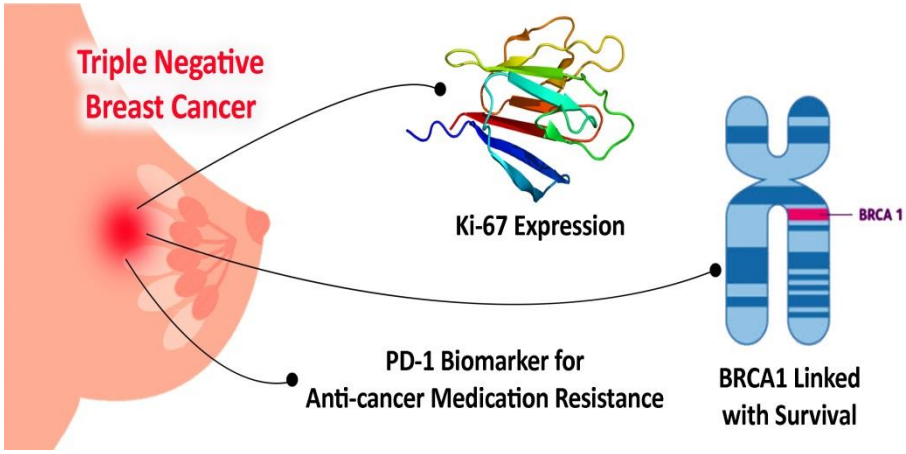
Highlights

- Ki-67 expression is closely related to the TNBC phenotype.
- BRCA1 promoter methylation has been linked to low overall survival in TNBC patients.
- PD-1 is a biomarker for anti-cancer medication resistance.

Graphical Abstract



Article Info

Receive Date: 25 February 2021
Revise Date: 30 March 2021
Accept Date: 13 April 2021
Available online: 21 April 2021

Keywords:
Triple-negative breast cancer
PARP inhibitors
Basal-like Breast cancer
HER2
BRCA1
BRCA2

Abstract

Triple negative breast cancer (TNBC) is a subtype of breast tumor which comprises 24% of newly diagnosed tumors that lacks hormone receptor expression and HER2 gene amplification. This study illustrated the pathological features of triple negative breast cancer with special reference to the landmark research that molecularly characterize this subtype of breast cancer. Additionally, this article discusses functional problems with arisen in clinical routine as a result of advent genetic expression breast cancer profiling and it's novel prognostic and predictive effects on triple-negative breast cancer pathology. Additionally, histopathological features of triple-negative neoplasms are discussed, emphasizing the critical nature of histologic detection in specific cancer subtypes with a significant effect on clinical results. Notably, emphasis is placed on the emerging clinical frontier represented by immunotherapy, with special emphasis on the implementation of immune checkpoint inhibitors in TNBC therapy and their effect on potential treatments.

10.22034/CAJMPSI.2021.02.05 **E-ISSN: 2783-0993**

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Introduction

TNBC is generally characterized by insufficient care and is therefore an interesting and complicated focus for study into breast cancer (1). In simplistic words, TNBC applies to several persons who have distinct biology and clinical features with various genomic, gene expression, histopathologic, and clinical distinctions (2, 3). A new approach for classifying breast tumors by gene expression sequence, termed genomic subtyping has been discovered using a technique called genomic subtyping (with triple-negative phenotype but also cellular derivation typical of normal breast epithelium). This classification, though comparatively recent, has been dubbed triple-negative (4). There is increasing realization of breast cancer clinical pathology's heterogeneity, demonstrated by the appearance of as many as five subtypes of breast cancer (5, 6). By following a surrogate clinical classification, in general, immunohistochemistry will become a modern and effective method for correctly testing the patients (7). Researchers are discovering more about genetic modifications in various kinds of breast cancer to introduce new genomic technology (8). Triple-negative breast cancers have progesterone receptor positivity, but lack estrogen receptor and HER2 positivity (9, 10, 11).

Histological pattern

Morphological and immunehistochemically characteristics should be used to research and understand TNBC. The IHC research plays a critical role in the concept of TNBCs and the proliferation of androgen receptor (AR), basal cytokeratin, and programmed death-ligand 1 (PD-L1).

Ki-67

About 20% of patients with early-stage TNBC have high Ki-67 expression. Higher Ki-67 expression was shown to be an independent prognostic factor for DFS (disease-free survival) (12, 13). Further, it has been shown that Ki-67 expression is closely related to the TNBC phenotype (14). The patients with Ki-67 expression less than 20% had worse survival than those with stable or increasing expression (15).

Androgen Receptor

For AR positivity, expression may vary from 9 to 90% (16, 17) for early TNBC identification, AR can be regarded as a biomarker. The positive AR expression enhances cell proliferation, while the negative AR expression suppresses cell growth (18). Two early-stage trials (phase II) have shown that abiraterone acetate plus prednisone and enzalutamide function for patients with AR-positive TNBC. Given these findings, antiandrogens synthesis in this subset has not been explored in-depth therefore Interest in this scenario is rising (19, 20).

EGF receptor

The epidermal growth factor receptor (EGFR) is essential in cell growth and cell death inhibition (21, 22). TNBC with irregular EGFR expression ranges from 13 to 78%. Controversy remains about evidence from EGFR protein overexpression in triple-negative cancer. Targeting this pathway has not yielded any great answer in clinical studies (23, 24).

Cytokeratins

Basal-like Breast cancer classically described as a basal cytokeratins aggressive subtype: CK 5/6, CK 14, and CK 17 (18). The expression of CK 5/6 in TNBC (25, 26) and CK 14 is between 24 and 72%, CK 17 also covers the same details as CK 5/6. Several observations led to the possibility that CK 5/6-positive TNBC have a bad prognosis; on the other hand, the CIBOMA trial indicated that a non-basal histomorphologic profile consistent with CK 5/6 and/or EGFR expression has better outcomes in addition CIBOMA's trial found that a non-basal expression by either CK 5/6 or EGFR of IHC contributes to a slightly improved overall survival (OS) and higher progression-free survival (PFS) when using capecitabine treatment (27).

Genomic alteration

Research investigating primary BC by genomic DNA copy number arrays, DNA methylation, exome sequencing, messenger RNA arrays, microRNA sequencing, and reverse-phase protein arrays were conducted by TCGA (Cancer Genome Atlas). The mutation burden of BRCA-mutated patients is higher than luminal cancers. TP53 mutations exist in 80% of TNBC, followed by PIK3CA mutations (9%) and other driver mutations (28).

TP53

TNBC has a 65 to 80% TP53 mutation rate. More studies show that the expression of p53 protein differs due to the type of mutation in the TP53 gene (29). Mutations in the p53 gene (found in nearly all cases of breast cancer) have little predictive utility as a prognostic or clinical tool for the condition and are considered as insignificant (30). The newly accessible molecules have renewed the mutant p53 protein and recovered the wild-type structure. Some of them have been tested in clinical trials and found to have anti-cancer properties (31). Besides, PTEN and INPP4B will affect serotonin AKT activation in 7 percent of TNBC. It's likely that the latest treatments will efficiently target this process (32). In patients with TNBC, the use of an AKT inhibitor with paclitaxel improved progression-free survival (PFS). Phase III clinical trials are currently ongoing for compounds like PI3K/AKT/mTOR (phosphoinositide 3-kinase/protein kinase B/mammalian target of rapamycin) pathway inhibitors. Additionally, owing to its anti-proliferative and immunosuppressive activities, PTEN (33) and INPP4B also have phosphatases, which may affect serotonin AKT activation in 7% of TNBC due to the cancer's continual, constitutive AKT activation. It might be possible to target this function with the latest therapies (34). In TNBC patients who harbored alterations in the AKT pathway, the addition of an AKT inhibitor to paclitaxel improved progression-free survival (PFS). There have been small gains in patient-provider contact. Compounds like AKT inhibitors are in the final stages of clinical trials (35).

BRCA

About twenty percent of TNBC people have a BRCA1/2 mutation (12% germline and 8% somatic). Similar to breast cancer, inherited tumors may also be caused by the BRCAness gene. The BRCA1/2 mutations' involvement and the disease known as BRCAness determine that a person will become more prone to platinum chemotherapy and be affected by some chemotherapeutic drugs (PARP). Both olaparib and talazoparib are recommended for first-line treatment for metastatic breast cancer with BRCA 1 or 2 based on randomized clinical trials (36, 37). In a small trial of talazoparib combined with BRCA1 or BRCA2 mutation-positive localized BC, the recurrence rate is 0 or 1 in 63% of them (38). Another accurate predictor of TNBC is DNA methylation (34, 39, 40). The TCGA was able to distinguish five distinct DNA methylation groups. Group 5 displayed a high prevalence of TP53 gene mutations along with a low degree of DNA methylation (41, 42). BRCA1 promoter methylation has been linked with low overall survival in TNBC patients (5).

Molecular Basis of Breast Cancer

Peru et al., researched genetic mechanisms of breast cancer that separated cancers into related physiologically different sub types (43, 44, 45). The term TNBC does not represent a person but is rather a collective diagnosis seen through genetic studies through molecular approaches (46). Among the first attempts to explicitly identify TNBC subtypes was a report in which researchers tried to see if the PMS50 intrinsic subtypes interacted with the molecular subtypes (47, 48). The RNA expression, somatic mutations, and copy number variation each display distinct patterns of modification in these subtypes. Neoadjuvant chemotherapy improved the cure rates of TNBC tumors (0 and 10%, respectively) (49). At least in the case of PAM50, it seems that Lehman subtypes will predict the PAM50 intrinsic subtypes better than PCR. Holmes et al., discovered that tumor-derived stromal cells impact the IM and MSL classifications, respectively. A number of genetic subtypes can be discovered by using this classification (BL1, BL2, M, and LAR) (50). Bl1 revealed 48% of TP53 mutations,

compared to 10% in BL2, 12% in M, and 15% in LAR. Burstein et al., observed that molecular TNBC could be more robust by using gene expression profiling. These forms were assigned unique names, which included LAR-like, MES-like, BLIS-like, and BLI-I. Creative usage: (BLIA) (51). Patients with the BLIS subtype were rated as having the worst prognosis, and patients with the BLIA subtype were ranked as having the best prognosis. Based on which molecular profiling methodology is used, there are four subtypes. The BL1 subtype has TP53 mutations (92%) that are present in its highest abundance, together with substantial amplification and gains of MYC and CDK6 (52). High Ki-67 mRNA expression correlates with a strongly proliferative nature. In the case of pluripotent stem cell proliferation disorders, such as BT, there is an elevated rate of pluripotent stem cell proliferation. Development factors such as EGF, NGF, MET, Wnt/β-catenin, and IGF1R must be present in high concentrations for BL2 syndrome to occur. Immune cell roles such as B- and T-cell receptor signaling, antigen presentation and cytokine pathways are all related to IM pathophysiology. The gene expression levels related to the epithelial-mesenchymal transition and the growth factor pathways are also increased in both mesenchymal tumor subtypes. Low expression of proliferation genes is observed in the MSL subtype. It is binding to stem cell-linked low expression of genes; BC is known to have lower speech of the following claudin family members: 3, 4, and 7. LAR have the highest clinical and genetic variability. In the hormonally regulated pathways (FOXA1 and GATA3), these ER-negative and overexpressed tumors exhibit elevated expression of AR mRNA and proteins. Almost all of the LUCC cells in the world have mutations in the gene products of PIK3CA, KMT2C, CDH1, NF1, and AKT1 (53).

Treatment

TNBC has few treatment choices, is vulnerable to recurrence and metastasis, and has a bad prognosis. Besides that, particular endocrine drugs and selective drug treatments are ineffective. Chemotherapy is the latest method for the treatment of TNBC. This protocol consisting of a mixture of taxane, anthracycline, cyclophosphamide, cisplatin, and fluorouracil is one of the recommended therapies. The drug is currently given along with chemotherapy for curing breast cancer. To choose effective chemotherapy and improve chemotherapy treatment, it is therefore essential to understand various chemotherapy regimens.

Taxanes

Taxel prevents microtubule depolymerization, which slows cell division and allows cells to remain in prometaphase. Taxel stimulates tumor development through activated macrophages. Taxel and taxane show different effects on tumor development, but both cause similar side effects (54). Commercially available solvents prepared using polyethoxylated castor oil as the solvent can cause serious or even catastrophic allergic reactions used in all processing sectors for storing taxel molecules Unlike the standard medication paclitaxel (i.e. sb-paclitaxel), Nab-paclitaxel (albumin-bound paclitaxel) would not need pretreatment to prevent allergic reactions and has a better drug distribution efficiency on endothelial cells (55). BL subtype had active expression of genes associated with growth and DNA repair (e.g., taxel or docetaxel).

When using taxane-based chemotherapy, four times higher treatment effectiveness rates were discovered for the BL1 and BL2 subtypes. Streptomyces peucetius var. is the cause of the antracycline antibiotics. Cesius will cure multiple kinds of cancer, including leukemia, lymphoma, breast cancer, uterine cancer, cervical cancer, and lung cancer. There are also appropriate dosing schedules for breast cancer, with the optimum dose of doxorubicin being 60 mg/m2, and that of epirubicin is 100 mg/m2 (56, 57, 58). Higher doses had no major impact on longevity or relapse rates. FEC-100 (100 mg/m2 epirubicin) regimens minimize the risk of recurrence by about 20–25% (59, 60). The age-adjusted mortality risk of those aged below 50 years decreased by about 38%, and that of those aged 50 to 69 years decreased by about 20% (61).

Cyclophosphamide

Cyclophosphamide reaches the body after it is activated by mixed-function oxidases in the liver. Acrolein alkylating material is generated by the activation of aldophosphamide in cancer cells. N-Mustard has cancer-

causing side effects. Taxol is the most effective regimen for HER2-negative breast cancer. Nakatsukasa et al. surveyed 52 breast cancer patients. 53.4% of the patients had four rounds of treatment taking four months with an overall progress rate of 16.3% (62).

TNBC breast cancer patients had a very high level of HPV DNA. Induction chemotherapy has few effects of TNBC treatment. Adjuvant treatment of women with node-negative breast cancer resulted in avoidance of local recurrence, which revealed a significant survival benefit (63). A retrospective analysis of reaction rates by TNBC subtype was performed by Masuda et al., Here, M1 accounts for 34.4% of the overall PCR. according to the PCR result, the BL1 subtype hit the highest rate, while the BL2, LAR, and MSL subtypes had the lowest 0, 10, and 23% $p = 0.022$ is also correlated with TNBC subtype Since there is this heterogeneity in TNBC, therapy needs to be varied (64).

Platinum agents

Cisplatin has anti-tumor efficacy (65). Cisplatin and Gemcitabine (GP) were to be the first-line treatment for advanced-stage TNBC in a phase II trial (NCT00601159) led by Zhang et al (mTNBC). It turned out that for patients with basal-like subtypes, as well as mTNBC, the treatment protocol was successful. An anti-cancer medication called carboplatin was used by Von Minckwitz to treat patients with their cancer (66, 67). Another way to say this is that in a study performed on patients with estrogen receptor-positive/androgen receptor-negative breast cancer, they found that the addition of carboplatin to standard antineoplastic chemotherapy and anthracycline chemotherapy triggered the reaction rate to significantly improve in those patients. Compared to other subtypes of TNBC, BL1-subtype TNBC was highly vulnerable to cisplatin chemotherapy (68).

Fluorouracil

Fluorouracil itself does not have any biochemical properties. Under the action of Orotate phosphoribosyltransferase, 5-Fluorouride monophosphate and deoxyuridine monophosphate is formed. Capecitabine is a cytotoxic agent that has selective anti-tumor action against cells. Eventually, Capecitabine itself has little cytotoxicity and is hugely useful after converting into 5-Fu in vivo. This activation is catalyzed by high thymidylate phosphorylase production in the tumor, contributing to a good (better than 5-FU) activity in tumor cells. Capecitabine works well for chemotherapy regimens that are not very effective at destroying the cancer cells. It has been an urgent issue in clinical practice because a growing number of breast cancer patients have developed resistance to anthracyclines and taxanes. Oral capecitabine only targets cancer cells that make pyrimidine. Capecitabine has excellent toxicity, efficacy, and management. In a study by Li et al., patients pretreated with anthracycline and taxane were given capecitabine and cisplatin combined therapy, and a substantial reaction was observed (69).

TNBC targeted counseling and potential treatment regimens. New treatments for this group of patients are being evaluated on immune-histochemical and genetic findings. Epidermal growth factor receptor (EGFR) Nielson et al., conducted a DNA microarray study of BLBC specimens and observed that approximately 60% of samples display elevated expression levels of EGFR. It was further confirmed that 70–78% of basal-like TNBCs indeed expressed EGFR. EGFR could be a promising target in TNBC. According to a randomized phase II trial, cetuximab treatment is unsuccessful, and the combined therapy of cetuximab with carboplatin only has a reaction rate of less than 30%. Most of the trials indicated a reduced survival risk in the patients treated with EGFR-targeted agents (70).

Cho and colleagues used a publically accessible gene expression dataset to define a cell population in which the ERBB pathway was activated. This suggests that bulk RNA-seq can detect differential expression in single-cell transcriptomes. It demonstrated heterogeneity within the tumor. It means that the molecular subtype of ERBB signaling is modified at the single-cell level. The EGFR pathway review findings found that the EGFR downstream pathways were still triggered in most TNBC patients following EGFR targeted therapy. There is a

desire for more therapies to attain significant effectiveness. After analyzing the gene expression profiling of Lehmann et al., (53).

PARP inhibitors

PARP1 is an important enzyme in the PARP family and is essential in DNA repair (71, 72). Decreased PARP activity can decrease DNA repair efficiency and cause cell death. With PARP antagonists, the efficacy of chemotherapy and radiotherapy can be greatly increased (73, 74). Of the PARP inhibitors, those with anti-tumor effects on BRCA1/2 deficient tumors had considerable anti-tumor effects on BRCA1/2 mutant tumors, while the PARP inhibitor effects on BRCA1/2 mutated tumors were more than thousands of times greater (Figure 1) (75). People with BRCA1/2 mutations that are of African descent have a slightly greater chance of inheriting BRCA1/2 mutations. The PARP inhibitors are produced with BRCA1 mutations in mind. Unfortunately, the target reaction time was not found in a recent clinical trial. Despite the lack of a statistically relevant difference in the probability of a response to paclitaxel between patients with and without known BRCA mutations, it suggests that paclitaxel administration presents a different degree of danger to patients with and without these mutations (76).

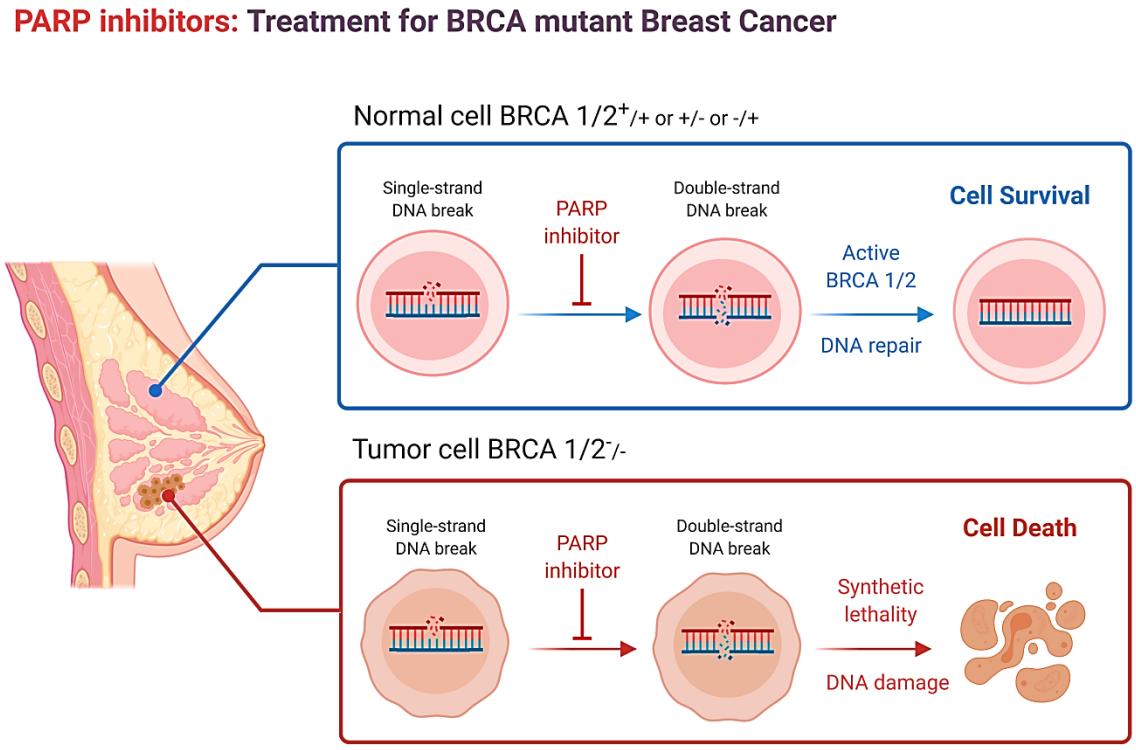

Figure 1. The PARP inhibitors have significant anti-tumor effects on BRCA1/2 deficient tumors.

Since it was expected that the existence of various repair mechanisms in women with TNBC could account for the resistance of these patients to doxorubicin, it was speculated that other repair mechanisms aside from PARP inhibitors could be at work in these women. While most study has shown that PI3K is important for controlling cell growth, metabolism, and cell survival, other studies indicate that it is also required for cell growth, metabolism, and survival (76). Combining a DNA disrupting agent with an inhibitor of PI3K reduces cell damage even further. A PI3K blockade has been shown to improve homologous recombination deficiency, as this makes BRCA1/2 decrease. Thus, PI3K blockade contributes to improved susceptibility to PARP inhibitor therapy in breast cancer. Conducting a study confirmed that in cancer patients who pair BKM120 with olaparib, the therapy is successful (NCT01623349). Prediction: BKM120 is likely to produce a tumor like that seen in women with BRCA mutations, rendering it resistant to PARP inhibition (77, 78, 79, 80). The results of Lehmann et al., (53) suggest that PARP inhibitors and DNA synthesis inhibitors can be helpful in the treatment of BL-1 cells, with a focus on the cell cycle and cell division pathways. Additionally, the sum of the androgen receptor

(AR) is distinct in standard and breast cancer tissues. AR can be found in approximately 10 to 15% of patients with TNBC (81, 82, 83).

Estrogen receptor ER- α 36

This approach may be suitable for LAR cell lines. There is a need for more experimentation and support for this new targeted regimen. Estrogen receptor-negative and ER, PR, and HER2 positive cells are known not to have a hormonal response (84, 85). They are naive of endocrine therapy and therefore ignore identifiable clinical targets, also EGFR and HER2 are part of the same family with strong structural and functional homology (Figure 2) (86). This is not something that has already been understood before. Compared with agonist, without the AF-1 and AF-2 domains and dimeric Agonist ER-α36 is primarily found in the cytoplasm and cell membrane of breast cancer cells. The ER-α36 can effectively mediate cellular responses to estrogen and antiestrogen signaling in breast cancer. Zhang et al., investigated the signaling of ER-α36 in TNBC cells and observed a positive feed-back loop of EGFR and ER-α36, showing the need for inquiry and care for TNBC. There is already much space for study (87).

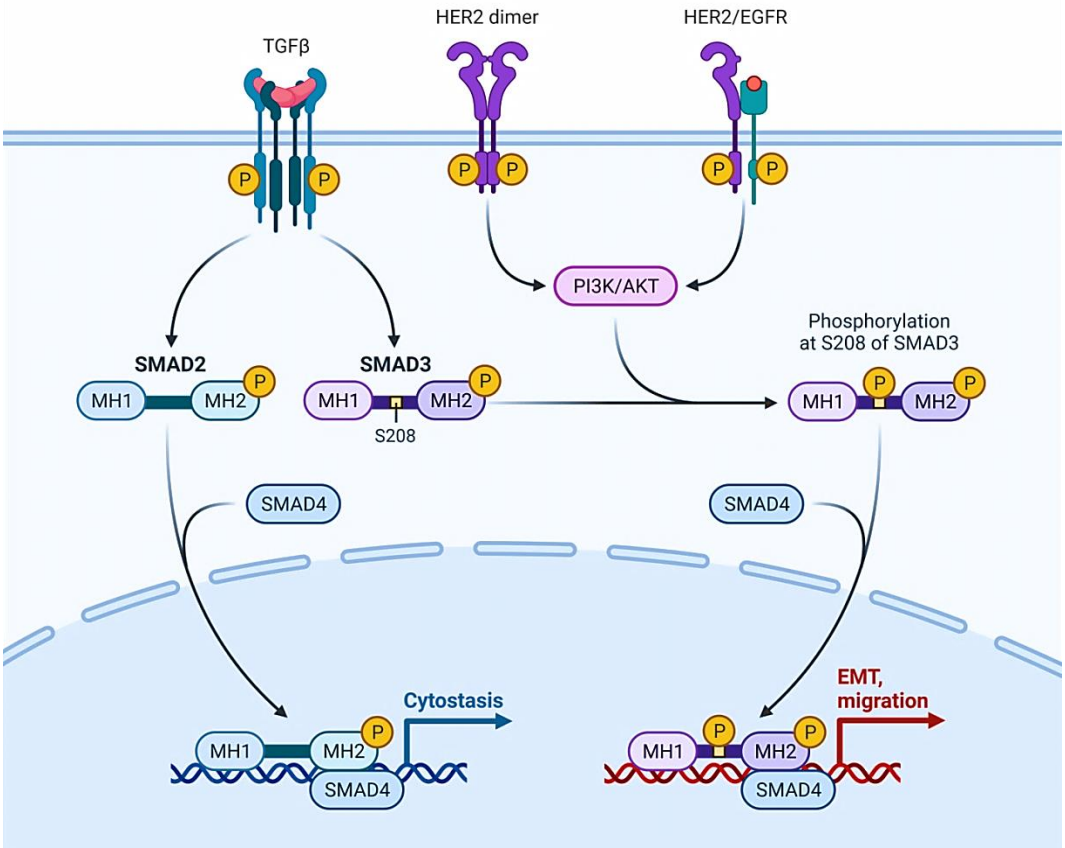

Figure 2. EGFR and HER2 are part of the same family with strong structural and functional homology.

Immunotherapy

The blocking of immune controls can play a major role in tumor treatment outcomes. PD-L1 is a 40,000 DMW glycoprotein that is located on the surface of cells. As normal body functions such as the immune system, the lymph nodes and spleen store antigens, the immune system reacts to these antigens. PD-1 is a biomarker for anti-cancer medication resistance. T cells are instructed to ignore tumor cells by binding PD-L1 to PD-1 on their surfaces (88, 89).

Tumor penetration and tumor grade are also associated with expression of PD-L1 and PD-1 (90, 91). Possible immunotherapy target for TNBC is PD-L1, as reported by researchers Sun et al., Non-small cell lung cancer (NSCLC) is the primary application of pembrolizumab, a PD-1 inhibitor (92, 93). In a phase I clinical trial, which used the anti-PD-L1 monoclonal antibody atezolizumab, the clinical response rate was approximately 10% (94).

The number of patients achieving long-term survival and a higher rate of long-term survival in patients treated with immune checkpoint inhibitors targeting PD-L1/PD-1 is relatively poor. The primary challenge of the day is to strengthen the care of PD-1 and PD-L1 in the treatment of TNBC patients and raise the number of responders to non-responders. That will offer an interesting chance for people suffering from advanced/metastatic TNBC because of the enhanced drug (95).

The immune response and the Ras/MAPK pathway have some link. Cancer cells use the Ras/MAPK pathway to prevent cancer antigens from being exposed to the immune system and to help cancer cells avoid death. CTLA-4 prevents T cell activation by binding CD80 and CD86. Ipilimumab is an antibody intended to keep melanoma at bay. There was an 11% drop in ORR for those who underwent ipilimumab monoclonal antibody therapy relative to control patients (96). The mixture of ipilimumab and nivolumab (PD-1 antibody) obtained a 61% ORR in Phase I clinical trials (NCT01927419) (97).

The results collected by analyzing combined therapy in advanced melanoma discovered that the drug had an average survival rate of 63.8% by using ipilimumab in combination with nivolumab (versus 53.6% when using ipilimumab alone) (98). Grade 3 and 4 adverse reactions resulted in a greater proportion of mixed patients than in those who administered monoclonal antibodies (59% vs. 20%). Colitis and diarrhea were among the 3 and 4 adverse events in the main categories of 3 and 4 adverse conditions. TNBC tumors and tumor cells were substantially cytotoxic when treated with a combination of anti-CTLA-4 monoclonal antibody and MUC1 mRNA nano vaccine (99). Bernier et al., greatly increased survival time in a mouse TNBC metastasis model, and integrating therapy promises considerable potential for efficient management of TNBC. T cell therapy based on unique chimeric antigen receptor (CAR) T cells is being used in the treatment of various immunological disorders (T cell therapy based on unique chimeric antigen receptor (CAR) T cells is currently being used in the treatment of various immunological disorders) (100, 101). Song et al., showed that CAR T cells modified to directly target FRα, which carried out reliable, active, and precise targeting of FRα-expressing human cancer cells in vitro, with the killing and inhibition results noted above (102, 103). Additional studies suggest that stem cells that lead FRα into MDA-MB-231 tumor xenografts-bearing immune-deficient mice have important anti-tumor effects. A glycopeptide (mesothelin) is a form of the protein present in mesothelium. Is present in mesothelial cells, this protein is only expressed (104, 105, 106).

Conclusion

TNBC carcinoma is highly invasive and has a high recurrence risk. Patients typically suffer a relapse and a much poorer overall prognosis after surgery. Clinical genomic testing would allow doctors to understand cancer's genetic origin even better as that would affect existing classification conventions. It is essential to differentiate high-grade from low-grade malignancy type of TNBC. Immunotherapy can lead to new opportunities for treating TNBC by combining immune checkpoint inhibitors with other therapeutic agents. Considering the high expression of ER, PR, and HER2, TNBC tumor is immune to hormone therapy and selective therapies. The only treatment options available for TNBC are poorly effective. New treatments are necessary now. A study on the use of AR in the treatment of TNBC also needs to be completed. There are plenty of mutant PI3K gene mutations in them. Therefore, targeting the PI3K signaling pathway may help patients suffering from LAR-subtype TNBC but is not successful for M-subtype TNBC. It is still unclear whether the M-subtype of TNBC has any other pathways affecting resistance to medication. Since its subtype (MSL) overexpresses receptors for vascular and endocrine growth factors, MSL is more resistant to anti-angiogenic medication. Immune-related genes and other markers are the significant distinctions between the IM subtype of TNBC and others. Immune checkpoint inhibitor therapies would most likely be helpful to the IM subtype. Both forms of TNBC except MSL display high frequencies of MYC gene amplification, while BL1 and M subtypes also show high levels of overexpression of mRNA. Selective inhibition of CDK1/2 and BUD31 can induce apoptosis of MYC-overexpressing TNBC tumor cells. Also, molecularly targeted therapies can be produced from mutants of multiple subtypes and types of TNBC. These subtypes have a high risk of genomic instability,

such as BRCA1 and RB1 gene deletion and PPAR1 gene amplification, indicating that these subtypes could be responsive to PARP Inhibitors. Unfortunately, expression levels of RB1, CDK4, and CDK6 are associated with susceptibility to CDK4/6 inhibitors. The bladder and Kidney may have opposing prognoses. BLIA has a higher survival rate than LAR, MES, and BLIS, while BLIS has the lowest survival rate. These results indicate that immune signals expressed in TNBC tumor cells and drug tolerance and prognosis expression interacted additionally, immune system antagonists may be used to treat BLIA subtype TNBC. ELF5, HOHMAD1, FOXC1, VTCN1, and SOX6 genes are upregulated in BLIS. Cancer immunotherapy with PD-1 or VTCN1 antibodies was planned. The findings of an investigation published in the Journal of Clinical Oncology showed that patients with a BL1 TNBC, along with the anti-cancer medications taxanes, anthracyclines, and platinum-based therapies, benefited from decreased residual disease levels following surgery. Due to the ambiguity of immunotherapy as a treatment of cancer, further experimental results are needed. Studies also showed that tumor-associated macrophages (TAMs) originating from peripheral-blood mononuclear cells were recruited into the tumor microenvironment as part of the host immune response. Tumor-infiltrating lymphocytes secrete inhibitory cytokines, which ultimately enhance the immune response to remove the cancerous cells effectively. This will permit concurrently upregulating PD-1 and PD-L1 expression in the tumor setting. Therefore, targeting TAMs for PD1/PDL-1-targeting drugs could be viable new suggestions. The creation of CAR-T immune therapies ought to be accompanied by a sufficient amount of statistical evidence. TNBC is now considered a disorder of intrinsic molecular subtype s and immunological heterogeneity, considering clinical phenotypes' diversity. The current scenario requires an immediate consideration of sub-classifications that integrate point-specific genetic signatures for more tailored and efficient therapy. Some success has been achieved with newly developed selective and different forms of checkpoint inhibitors in recent years. A more substantial panel of immune histochemical molecular subtypes was a foundation of the judgment in the treatment of TNBC. A better molecular classification would give doctors more precise knowledge to control patients' chemotherapy therapies. TNBC a once-unimaginable parasite and is now successfully handled using molecular medicine. With improvements in subtypes of the disorder and the combination of immunotherapy and selective inhibitors, significant success has been made in the treatment of TNBC.

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How to cite this paper:
Miri A, Kiani E, Habibi S, Khafaei M. Triple-negative breast cancer: biology, pathology, and treatment. Cent Asian J Med Pharm Sci Innov 2021; 1(2): 81-96.