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Letter to the Editor

What is the future in the treatment of triple-negative breast cancer?

Dear Editor,

Triple-negative breast cancer (TNBC) is generally a subgroup of poorly differentiated immunohistochemically (IHC) estrogen (ER), and progesterone receptor (PR) negative breast cancers. Based on gene expression analyses, it is included in the basal-like subgroup. However 'basal-like group' is not directly the equivalent of 'triple negative group'. Fifteen percent of immunohistochemically triple-negative group may not be a basal-like subtype in gene expression analysis or vice versa. TNBC is the most heterogenous group among breast cancer subtypes. They do not benefit from hormonal treatments since they are ER, and PR negative, and from anti-HER2 treatment because they are HER2-negative. Therefore neoadjuvant, adjuvant, and during metastatic stage systemic chemotherapy (priorly anthracycline, and taxane-based drugs) have been recommended. Well, then do new targets for the treatment of TNBC still exist?

According to Vanderbilt classification for TNBC, TNBC has subgroups as follows: 'basal-like 1' (BL1), 'basal-like 2' (BL2), 'immunomodulatory' (IM), 'mesenchymal like' (M), 'mesenchymal stem-like' (MSL), and luminal androgen receptor (LAR). Among these subgroups BL2, and M have a worse, and BC1, LAR, and IM better prognoses.[1] Activities of EGFR, and MET pathway in BL2, immune pathway in IM, and androgen-receptor (AR) pathway in LAR subgroups, and abnormal DNA repair genes in BL1 were detected.[2] In TNBC, addition of iniparib (PARP inhibitor) to chemotherapy (carboplatin-gemcitabin) prolonged PFS, and OS for 2.3, and 4.6 months, respectively when compared with chemotherapy *per se*.[3] Among studies with androgen receptor antagonists, in the TBCRC 011 study, clinical benefit was detected in 19% of the patients, and PFS was extended up to 12 weeks.[4] However in the MDV 3100-11 study, with enzalutamide used at daily doses of 160 mg clinical benefit was obtained in 42% of the patients and median PFS was 16 weeks.[5] In approximately 20–60% cases of triple-negative breast cancer PD-L1 expression is detected. Lymphocytic infiltration in the triple breast cancer tissue is related to improved prognosis. In KEYNOTE-012 phase I study which is among immunotherapuetic investigations, 32 metastatic TNBC patients with PD-L1 positivity received 10 mg/kg IV pembrolizumab. Rates of overall (18.5%), complete (3.7%) and partial (14.8%) response rates, and stable disease (25.9%) were also estimated as indicated.[6] As a conclusion targeted therapies for breast cancer subtype of TNBC exist. In the treatment of TNBC especially PARP inhibitors, AR antagonists, and immunotherapy are promising treatment modalities.

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