Additional biomarkers for pathological complete response in triple negative breast cancer

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Dear Editor,

We read your letter titled 'Assessment of novel prognostic biomarkers to predict pathological complete response in patients with non-metastatic triple-negative breast cancer using a window of opportunity design' with great interest.[1]

Apart from the biomarkers discussed in the above journal article, we feel that BReast CAncer gene 1 (BRCA1) is also an important biomarker to predict pathological complete response (pCR) in triple negative breast cancer (TNBC). It is noted that not all BRCA1 positive breast cancers are triple negative. However, in those with BRCA1 mutations, 57% are triple negative, and they are associated with higher nuclear grade.[2] Jia et al.[3] suggested that platinum-based chemotherapy should be used in BRCA1 and 2 TNBC patients to improve objective remission rate and survival rate. An increase of up to 17.6% in pCR is reported among patients receiving platinum-based chemotherapy in the treatment of TNBC with BRCA1 and 2, thus improving overall prognosis significantly.[3] This suggests that BRCA status is important to guide treatment in patients with TNBC.

Programmed cell death protein ligand 1 (PD-L1) expression is also another established predictor marker of pCR rate. PD-L1 is known to contribute to the mechanism of immune escape and immune cell infiltration. The three identified PD-L1 antibodies used for prognostication are SP142 Ventana, 22C3 and SP 263. In this review, it is found that 50–80% of all TNBC tumours were PD-L1 positive based on a cut-off of more than 1% on immunohistochemical staining for any of the three antibodies.[4] The same review also showed evidence that PD-L1 blockade produces an anti-tumour immune response, improving prognosis of its cohort. Future research on PD-L1 blockade medications can prove to be beneficial and provide aid in the treatment of TNBC patients.

In the case of TNBC, Cluster of Differentiation (CD)73 is also another significant marker for prognosis prediction. It is understood that in the tumour microenvironment, CD73 expression contributes to the production of immunosuppressive extracellular adenosine, promoting tumour immune escape. In a study by Buisseret et al.[5] which is conducted on 122 paraffin-embedded TNBC tumour samples, evidence suggests that high levels of CD73 expression on epithelial tumour cells is associated with a poor prognosis and reduced anti-tumour immunity.

This meta-analysis by Van den Ende et al.[4] reported that low levels of CD 73 expression on tumour cells correlates with an increased pCR rate. This analysis also found significant evidence of combining three markers, PD-L1, CD73 and Tumour-Infiltrating Lymphocytes (TILs), to improve prediction of pCR.[4]

Next-generation sequencing (NGS) is a relatively new method to sequence oncogenes and to evaluate for actionable mutations. In the near future, NGS may contribute in classification, treatment, prognosis as well as evaluation of drug resistance in cases of TNBC. The advantage of NGS is that it can be performed on both tumour tissue and circulating tumour DNA from blood samples.[6] Future studies can look into incorporating NGS and all the other available markers into development of a composite prognostic score for more accurate assessment of pCR among TNBC patients.

Declarations

Authors' note
All authors freely agreed for publication should this manuscript be accepted.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

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