Clinicopathological and prognostic significance of programmed death-ligand 1 expression in patients diagnosed with breast cancer: a systematic review and meta-analysis

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Background: Programmed cell-death ligand 1 (PD-L1) is a protein expressed at varying levels on the surface of cancer cells. Uncertainty exists regarding its relevance in breast cancer (BC). We aimed to perform a systematic review and meta-analysis evaluating the clinicopathological and prognostic role of PD-L1 in BC.

Methods: A systematic review was performed in accordance to PRISMA and MOOSE guidelines. Observational studies that compared high versus low expression of PDL-1 on BC cells were identified. Log hazard ratios (lnHR) for disease-free survival (DFS) and overall survival (OS) and their standard errors were calculated from Kaplan-Meier curves or cox-regression analyses and pooled using the inverse variance method. Dichotomous variables were pooled as odds ratios (OR) using the Mantel–Haenszel method.

Results: Sixty-five studies of 19,870 patients were included; 14,390 with low- and 4,989 with high-PDL-1 expression. High PD-L1 was associated with grade 3 tumours (OR: 2.16, 95% CI: 1.64–2.83, P<0.01, I²=82%), estrogen receptor negativity (OR: 2.29, 95% CI: 1.54–3.41, P<0.01, I²=89%), progesterone receptor negativity (OR: 2.44, 95% CI: 1.69–3.51, P<0.01, I²=83%), Ki-67 expression >14% (OR: 2.12, 95% CI: 1.23–3.65, P<0.01, I²=89%) and achieving pathological complete response (pCR) following neoadjuvant chemotherapy (NAC) (OR: 3.31, 95% CI: 1.20–9.11, P<0.01, I²=85%). Low PD-L1 was associated with human epidermal growth factor receptor-2 (OR: 3.98, 95% CI: 1.81–8.75, P<0.01, I²=96 percent) and luminal (OR: 14.93, 95% CI: 6.46–34.51, P<0.01, I²=99%) molecular subtypes. Those with low PD-L1 had favourable OS rates (hazard ratio: 1.30, 95% CI: 1.05–1.61, P<0.01, I²=85%).

Conclusions: BCs with high PD-L1 expression are associated with aggressive clinicopathological and immunohistochemical characteristics and are more likely to achieve pCR following NAC. However, they are associated with worse OS outcomes.

Keywords: Breast cancer (BC); personalised medicine; patient outcomes

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Footnote
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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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