

THE STUDY OF PROGRAMMED DEATH-1 RECEPTOR, PROGRAMMED DEATH-1 LIGAND (PD-1/PD-L1) AND APOPTOSIS IN BREAST CANCER PATIENTS: A POTENTIAL MECHANISM OF IMMUNE ESCAPE

Ali, S.A¹, El-Daly, A.N², El-Sayed, A³, El-Shredy, H.G⁴, Fadaly, G.A⁵

¹Medical Research Institute, Alexandria University, Alexandria City, Egypt, ²Faculty of Pharmacy, October University for Modern Science and Arts (MSA), October City, Giza, Egypt, ³Department of Immunology and Allergy, Medical Research Institute, University of Alexandria, Alexandria City, Egypt, ⁴Department of Cancer Management and Research, Medical Research Institute, University of Alexandria, Alexandria City, Egypt, ⁵Department of Pathology, Medical Research Institute, University of Alexandria, Alexandria City, Egypt

Introduction: The associations between programmed cell death ligand 1 (PD-L1) and the prognosis of various cancers have always been a research topic of considerable interest. However, the prognostic value of PD-L1 in breast cancer patients remains a controversial subject. We aimed to evaluate the role of programmed death-1 receptor and programmed death ligand-1 (PD-1/PD-L1) expressing lymphocytes, monocytes and granulocytes, as potential mechanism of immune escape in breast cancer patients. Also, serum levels of Bcl-2 were analyzed among patients with different stages of breast cancer.

Material and Methods: The study was conducted on a total of seventy-five females; fifty-five of them represented the breast cancer females at early (24 females) and advanced (31 females) stages and 20 age matched female donors

represented the control group. Patients were recruited from the Cancer Research and Management Department, Medical Research Institute, Alexandria University. Venous blood samples obtained from all females under study were used for determination of PD-1/PD-L1 expression using flowcytometry technique and measurement of Bcl-2 serum levels using ELISA technique.

Results: Significantly higher expression levels of PD-L1 were found in patients with positive lymph node, advanced tumor stage, histological grade II, tumor size T2, ER, PR, Her-2 negativity and TNBC subtype. Whilst a general increase in PD-1 positive expression between the breast cancer patients and control group regarding percentage and MFI of positive PD-1 expressing monocytes and granulocytes. Also, the results showed a highly significant association between PD-1+ and PD-L1+ expression in early and advanced breast cancer patients ($p < 0.0001$). There was a significant increase in the mean of Bcl-2 serum concentration in patients compared to healthy individuals. Finally, the results showed that Bcl-2 serum concentration correlated positively with positive PD-L1+ expressing granulocytes. While the correlation between serum Bcl-2 and PD-1+ expressing lymphocytes, monocytes and granulocytes did not show any statistical significance.

Conclusions: Our study suggested that PD-L1 could serve as an important target for antibody based immunotherapies, especially in the TNBC, where treatment options are limited. The direct correlation between PD-L1+ expression and serum Bcl-2 concentration may explore a role of apoptotic machinery in the pathogenesis of breast cancer.