http://dx.doi.org/10.7124/bc.000AC8

Association of genetic alterations in the EGFR and ALK genes with PD-L1 expression in non-small cell lung cancer

Yu.V. Moskalenko[1], D.S. Kozakov[2], S.S. Livshun[2], M.I. Panko[2], O.M. Sulaieva[2]

[1] Sumy State University
116, Kharkivska Str., Sumy, Ukraine, 40007
[2] Medical Laboratory CSD, Kyiv, Ukraine
22B, Zhmerynskaia Str., Kyiv, Ukraine, 03148
yl.moskalenko@med.sumdu.edu.ua

Introduction. In recent decades, immunotherapy has become important for treating the non-small cell lung cancer (NSCLC) patients. However, specific genetic alterations limit the response to immune checkpoint inhibitors even in the presence of PD-L1 expression. The study aimed to evaluate the relationship between genetic disorders in the EGFR and ALK genes and PD-L1 expression in NSCLC patients. **Methods.** The study was performed on 117 samples from patients with NSCLC, among which there were 95 adenocarcinomas and 22 squamous cell carcinomas. All patients provided informed consent. Research on the molecular profile of tumors was carried out using next-generation sequencing (NGS; NexSeq550, Illumina). PD-L1 expression was assessed by immunohistochemistry (IGH, clone 22C3, Dako) based on TPS determination. PD-L1 expression <1% was evaluated as negative (PD-L1^{-}), PD-L1 from ≥1% to 49 was considered positive (PD-L1^{+low}), expression ≥50% was interpreted as strongly positive (PD-L1^{+high}). Statistical analysis was performed using MedCalc® version 22.016. The χ^2 criterion was used to compare the frequency of different variants of PD-L1 expression in different genetic alterations. A P-value < 0.05 was considered statistically significant. **Results.** Negative expression of PD-L1 was determined in 51 cases (43.6%) among 117 samples of NSCLC. Positive expression of PD-L1 was registered in 66 cases, among which 45 carcinomas (38.5%) had the status PD-L1^{+low} and 21 (17.9%) – PD-L1^{+high}. When assessing the frequency of genetic alterations in the NSCLC, EGFR mutations were found in 17 patients (14.5%) and ALK rearrangement in 8 cases (6.8%). When analyzing the relationship between genetic alterations and PD-L1 expression, a higher frequency of PD-L1 expression was found in the EGFRm tumors (χ^2=7.58; P = 0.02). Among 17 NSCLC with mutations in the EGFR gene, three were PD-L1-negative, and 14 were PD-L1 positive (10 — PD-L1^{+low}, 4 — PD-L1^{+high}). In contrast, over half of EGFRwt lung carcinomas (52 of 100) were PD-L1^{-}. Similarly, 7 of 8 NSCLCs with ALK rearrangements were also PD-L1 positive, in contrast to carcinomas without ALK disorders (χ^2 = 5.19; P = 0.037). Given that the presence of the EGFR and ALK genetic disorders determine resistance to immunotherapy with immune checkpoint inhibitors. Molecular testing of these genes is a mandatory prerequisite for personalizing the treatment of NSCLC patients. **Conclusions.** Mutations in the EGFR gene and ALK rearrangement are associated with the activation of PD-L1 expression. Therefore, mandatory molecular testing to personalize the treatment of NSCLC patients is needed.

Keywords: lung cancer, next-generation sequencing, PD-L1, EGFR, ALK.