Pd-1 and pd-l1 gene expression analysis in peripheral blood mononuclear cells in non-small cell lung cancer: association with kras mutation status and patient prognosis

Abstract Submitter: Kleita Michaelidou, Greece*

Co-Authors: Vassilios Vagiatis, Chara Koutoulaki, Anastasios V. Koutsopoulos, Aristeidis E Boukouris, Konstantinos Svoliantopoulos, Athina Kyriakidou, Maria A. Papadaki, Dimitrios Mavroudis, Sofia Agelaki

*Laboratory of Translational Oncology, School of Medicine, University of Crete

Abstract

Background: The PD-L1/PD-1 axis plays a crucial role in cancer immune evasion. KRAS mutations have been shown to upregulate PD-L1 expression, enhancing immunosuppression and contributing to tumor progression. While studies have primarily focused on the tumor microenvironment, liquid biopsy-based assessments of tumor-induced systemic immune disruptions remain limited.

Objective: This study aimed to evaluate the PD-1 and PD-L1 mRNA expression in peripheral blood mononuclear cells (PBMCs) according to KRAS mutation status and assess their prognostic significance in non-small cell lung cancer (NSCLC) patients.

Methods: A total of 128 NSCLC patients receiving first-line therapy at the University General Hospital of Heraklion were included. PBMCs were isolated using Ficoll density gradient centrifugation, and total RNA was extracted. Quantitative real-time PCR was performed for the target genes using PGK1 as the reference gene. Relative expression levels (2-ΔCT) were calculated and analyzed statistically.

Results: PD-L1 (p=0.023) and PD-1 (p=0.033) expression in PBMCs correlated positively with age. PD-L1 (p=0.014), but not PD-1 (p=0.402) expression was higher in female patients. No significant differences in PD-L1 (p=0.212) or PD-1 (p=0.473) expression in PBMCs were observed between patients with and without KRAS mutations in tumor tissue. Similarly, no associations were found between PD-L1 (p=0.625) or PD-1 (p=0.795) expression in PBMCs and PD-L1 expression in tumor tissue. Kaplan-Meier analysis showed that high PD-L1 expression in PBMCs (cutoff: 50th percentile, p=0.034) was associated with significantly longer overall survival (OS), whereas PD-1 expression showed no significant association with OS (p=0.062). KRAS mutation status and PD-L1 expression in tumor tissue were not associated with OS outcomes. Multivariate analysis confirmed high PD-L1 expression in PBMCs as an independent prognosticator of favorable OS in NSCLC (HR=0.604; p=0.029), irrespective of KRAS mutation status.

Conclusion: PD-L1 expression in PBMCs emerges as a promising non-invasive biomarker for NSCLC patients. These findings highlight the potential of liquid biopsy-based systemic immune profiling as a complementary approach for prognostic assessment. Further studies are warranted to validate these results and investigate the expression of other immune checkpoint molecules and their impact on patient prognosis.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.