UDK 616.233-006.6-036.8 **Original Scientific Paper**
Doi 10.7251/SANUS2503111M

ASSOCIATION OF CLINICOPATHOLOGICAL CHARACTERISTICS AND PD-L1 EXPRESSION IN PATIENTS WITH SQUAMOUS CELL LUNG CANCER

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Abstract. *Squamous cell lung cancer does not always respond well to standard oncological treatments. Current research is largely focused on immunotherapy targeting immune checkpoints. Assessing the expression level of PD-L1 (programmed death-ligand 1) is a necessary prerequisite for considering treatment with monoclonal antibodies that inhibit the PD-1/PD-L1 signaling pathway. The aim of this study is to determine the association between PD-L1 expression in squamous cell lung cancer and clinicopathological characteristics, including gender, age, smoking status, tumor laterality, TNM stage, and ECOG performance status, in patients treated at the Institute for Pulmonary Diseases of Vojvodina. This retrospective study included 94 patients of both sexes diagnosed with squamous cell lung cancer between January 1 and December 31, 2021. Diagnosis was based on histopathological analysis, with additional immunohistochemical assessment of PD-L1 expression. Positive PD-L1 expression (>1%) was observed in 78.7% of patients, while 52.1% showed high expression levels (>50%). Multivariate analysis revealed no statistically significant association between PD-L1 expression and gender (p=0.845), tumor localization (p=0.670), smoking status (p=0.323), or TNM stage (p=0.603). A statistically significant association was found between PD-L1 expression <1% and ECOG performance status (p=0.035). A marginal association was observed between PD-L1 expression >50% and patient age (p=0.058). PD-L1 expression in squamous cell lung cancer patients does not appear to be significantly associated with most clinicopathological characteristics. However, patient age and ECOG performance status may suggest variations in PD-L1 expression. Further studies with larger sample sizes are needed to draw definitive conclusions.*

Key words: *Squamous cell lung cancer; PD-L1 expression; Predictive biomarker; Clinicopathological characteristics*

Introduction

Bronchial carcinoma is among the most aggressive neoplasms in oncology. It remains the leading cause of cancer-related mortality worldwide in both men and women, accounting for more than 1.8 million deaths annually [1]. In Serbia, lung cancer incidence and mortality are among the highest in Europe, with survival rates remaining low due to late-stage diagnosis [2]. The main etiological factor is tobacco smoking, while environmental exposures such as air pollution and occupational hazards also contribute to disease development [3].

Bronchial carcinomas arise through the stepwise accumulation of genetic and epigenetic alterations that drive malignant transformation of epithelial cells [4]. In parallel with advances in molecular oncology, the role of the immune system in tumor progression and treatment has been increasingly recognized. A key mechanism of immune evasion in non-small cell lung carcinoma (NSCLC) involves inhibitory immune checkpoint pathways, particularly the programmed cell death protein 1 (PD-1) and its ligand PD-L1 [5]. PD-L1, identified in 1999, is broadly expressed on tumor and immune cells, where its interaction with PD-1 attenuates T-cell activation, promotes immune tolerance, and facilitates tumor progression [6–8]. Its expression is heterogeneous and modulated by the tumor microenvironment, further complicating interpretation [7, 9].

Therapeutic blockade of the PD-1/PD-L1 axis with monoclonal antibodies such as pembrolizumab and nivolumab has significantly improved clinical outcomes in selected NSCLC populations, especially in tumors with high PD-L1 expression (≥50%) [12–14]. Accordingly, PD-L1 is regarded as a clinically relevant predictive biomarker, and its evaluation by immunohistochemistry is recommended prior to immunotherapy initiation, despite limitations posed by intra- and intertumoral heterogeneity [11].

While targeted therapies have revolutionized the management of adenocarcinoma, comparable advances have not been achieved in squamous cell carcinoma (SCC), underscoring the importance of PD-L1 assessment in this histological subtype [13, 14].

Despite the therapeutic promise of immunotherapy, its application remains limited to select patient groups. Unrestricted use can significantly increase the risk of adverse events [15]. Investigating tumor–host interactions and identifying predictive biomarkers in correlation with clinicopathological characteristics is essential for enhancing the efficacy of immune checkpoint inhibitors. This study aimed to examine the relationship between PD-L1 expression and clinicopathological characteristics in patients with squamous cell lung carcinoma.

Materials and methods

This retrospective study was conducted by reviewing medical records from the Institute for Pulmonary Diseases of Vojvodina (IPDV) in Sremska Kamenica, covering the period from January 1 to December 31, 2021. Histopathological samples were processed at the Department of Pathology and Molecular Diagnostics, and data

were extracted from the institutional electronic health record system (JZIS). Variables included demographics, smoking status, histological type of bronchial carcinoma, tumor laterality, PD-L1 expression, TNM stage (8th edition), and ECOG Performance Status (0–2 scale). The study was approved by the Ethics Committee and the Scientific Council of the Institute for Pulmonary Diseases of Vojvodina.

Participants

Data from 94 patients aged 48 to 81 years, with a histopathologically confirmed diagnosis of squamous cell carcinoma of the bronchus, were analyzed.

Inclusion criteria:

- Age 18 years or older
- Histopathologically confirmed squamous cell carcinoma of the bronchus
- Adequate tissue sample available for testing

Exclusion criteria:

- Age under 18 years
- Other histological subtypes of NSCLC or small cell lung cancer (SCLC)
- Inadequate tissue for testing

Tissue sampling and histopathological processing

Tumor samples were obtained predominantly by bronchoscopy and, less frequently, by lobectomy. Specimens were processed using standard histopathological protocols, embedded in paraffin, sectioned at 4 μm, and stained with hematoxylin and eosin (H&E).

Immunohistochemical analysis

Representative sections containing at least 100 viable tumor cells were stained with a commercial anti–PD-L1 antibody (Clone 22C3, Dako). PD-L1 expression was assessed by the Tumor Proportion Score (TPS) and classified as <1%, 1–49%, or ≥50%; any membranous staining in >1% of viable tumor cells was considered positive.

Statistical analysis

Numerical variables were presented as means (arithmetic means) and standard deviations, while categorical variables were reported as frequencies and percentages. Univariate analysis included the use of the chi-squared test (χ^2) and Student's t-test. A p-value of <0.05 was considered statistically significant. Data analysis was performed using IBM SPSS Statistics version 21.

Results

The study covered a one-year period, from January 1 to December 31, 2021. The total number of patients treated for squamous cell carcinoma of the bronchus during this period, whose tumor tissue was immunohistochemically tested for PD-L1 expression, was 94. Males constituted the majority of participants, while females represented a minority (Table 1).

Table 1. Gender distribution of participants

	Number of participants	Percentage (%)
Male	68	72,3
Female	26	27,7
Total	94	100,0

Regarding tumor location, 46.8% had a tumor on the right side, and 53.2% on the left. Based on personal medical history, participants were stratified into three groups according to cigarette consumption. Smokers constituted the largest group, with Table 2 detailing the numerical and proportional distribution across all categories.

Table 2. Distribution of non-smokers, smokers, and former smokers

	Number of participants	Percentage (%)
Non-smokers	7	7,4
Smokers	60	63,8
Former smokers	27	28,7
Total	94	100,0

A pie chart illustrates the numerical data on participants' distribution based on the ECOG Performance Status scale (Chart 1) and TNM stage (Chart 2). The study included participants of all stages of squamous cell carcinoma of the bronchus.

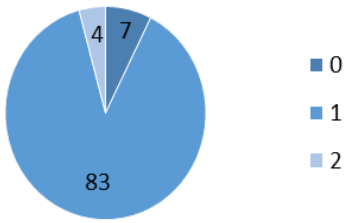

Chart 2. Number of participants by ECOG Performance Status scale

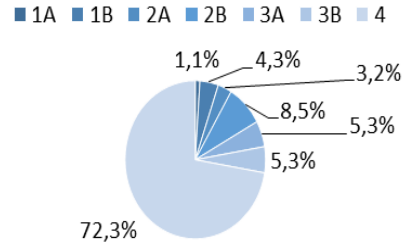

Chart 1. Distribution of participants by TNM classification

The highest number of participants had PD-L1 tumor cell expression in the 1–49% range, with 49 individuals (52.1%). The distribution of participants by percentage of PD-L1 tumor cell expression is presented in Table 3.

Table 3. Distribution by percentage of PD-L1 tumor cell expression

	Number of participants	Percentage (%)
<1%	20	21,3
1−49%	**49**	**52,1**
>50%	25	26,6
Total	94	100,0

Among participants with PD-L1 expression >50%, the mean expression was 72.24% (95% Confidence Interval: 66.64–78.02).
There is a marginal statistical association between PD-L1 expression >50% and age (p=0.058). The relationship is presented in Table 4.

Table 4. Relationship between age and PD-L1 expression

		N	**Mean value**	**95 % Confidence Interval**	
				Lower limit	Upper limit
Age	<1%	20	65,20	61,83	68,57
	1−49%	49	68,41	66,33	70,49
	>50%	25	64,44	61,29	67,59
	Total	94	66,67	65,14	68,20
Percentage of tumor cell positivity	<1%	20	,00	,00	,00
	1−49%	49	13,90	9,88	17,92
	>50%	25	72,24	66,46	78,02
	Total	94	26,46	20,15	32,77

Legend: N – number of participants.

Multivariate analysis showed no association between PD-L1 expression and gender (p=0.845), as shown in Table 5.

Table 5. Relationship between PD-L1 expression and gender

			Gender		Total
			Male	Female	
Percentage of tumor cell positivity	<1%	N	15	5	20
		Percentage (%)	75,0	25,0	100,0
	1−49%	N	36	13	49
		Percentage (%)	73,5	26,5	100,0
	>50%	N	17	8	25
		Percentage (%)	68,0	32,0	100,0
Total		N	68	26	94
		Percentage (%)	72,3	27,7	100,0

Legend: N – number of participants.

There was no statistically significant association (p=0.670) between tumor cell PD-L1 expression and tumor laterality (Table 6).

Table 6. Relationship between PD-L1 expression and tumor laterality

			Location		Total
			Right	Left	
Percentage of tumor cell positivity	<1%	N	8	12	20
		Percentage (%)	40,0	60,0	100,0
	1−49%	N	25	24	49
		Percentage (%)	51,0	49,0	100,0
	> 50%	N	11	14	25
		Percentage (%)	44,0	56,0	100,0
Total		N	44	50	94
		Percentage (%)	46,8	53,2	100,0

Legend: N – number of participants.

In the multivariate analysis, cigarette smoking status did not show a statistically significant association with the percentage of PD-L1 tumor cell expression. However, distributional trends across smoking categories suggest potentially relevant patterns. Among non-smokers, 15.0% (3 patients) had PD-L1 expression <1%, 8.2% (4 patients) had expression between 1–49%, and none exhibited expression >50%. In contrast, within the group of current smokers, 50.0% (10 patients) had expression <1%, 65.3% (32 patients) had expression 1–49%, and 72.0% (18 patients) showed high expression levels >50%. Although not statistically significant, this numerical predominance of smokers in the high-expression group suggests a potentially meaningful trend. Among former smokers, 35.0% (7 patients) had expression <1%, 26.5% (13 patients) had 1–49%, and 28.0% (7 patients) had expression >50%.

A statistically significant association was found between ECOG Performance Status and PD-L1 expression <1% (p=0.035). Among participants with ECOG score 0, 15% had <1% expression, 4.1% had 1–49%, and 8% had >50% expression. These data suggest a possible link between lower ECOG status and lower PD-L1 expression.

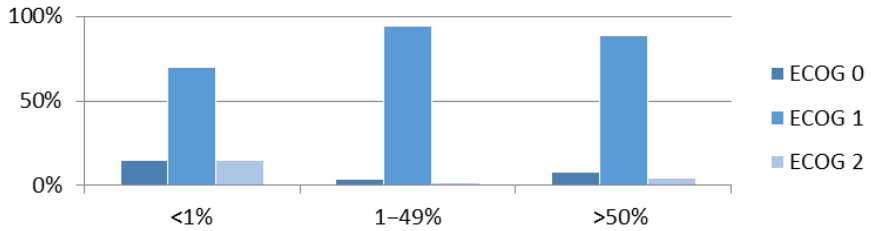

Chart 3. Relationship between ECOG Performance Status and PD-L1 tumor cell expression

There was no statistically significant association between PD-L1 expression and TNM stage (p=0.603), as shown in Table 7.

Table 7. Relationship between PD-L1 expression and TNM stage

			TNM Stage						
			1A	1B	2A	2B	3A	3B	4
Percentage of tumor cell positivity	<1%	N	0	2	1	2	2	1	12
		Percentage (%)	0,0	10,0	5,0	10,0	10,0	5,0	60,0
	1−49%	N	0	2	2	3	1	3	38
		Percentage (%)	0,0	4,1	4,1	6,1	2,0	6,1	77,6
	>50%	N	1	0	0	3	2	1	18
		Percentage (%)	4,0	0,0	0,0	12,0	8,0	4,0	72,0
	Total	N	1	4	3	8	5	5	68
		Percentage (%)	1,1	4,3	3,2	8,5	5,3	5,3	72,3

Legend: N – number of participants

Discussion

As the global burden of non-small cell lung cancer (NSCLC) continues to rise, the implementation of novel and more effective therapeutic strategies has become imperative. Recently published and presented clinical trials continue to support the efficacy of immune checkpoint inhibitors [9, 15, 16]. Evidence suggests that clinical outcomes are improved in patients whose tumors exhibit elevated PD-L1 expression levels.

Enhancing cost-effectiveness through patient selection based on PD-L1 expression assessment may significantly contribute to the rationalization of therapeutic approaches from a clinical standpoint [17]. This allows for the identification of patients most likely to benefit from specific treatments, thereby optimizing therapeutic outcomes and reducing unnecessary healthcare costs. Accurate patient selection enables more efficient use of immune checkpoint inhibitors, which not only increases therapeutic efficacy but also reduces the risk of adverse events associated with unregulated use of these agents. This ensures appropriate and sustainable use of advanced targeted therapies.

Several research groups have investigated the relationship between PD-L1 expression and clinical variables such as sex, smoking history, histological subtype, tumor invasion grade, TNM stage, and response to various treatment modalities. However, the correlation between PD-L1 expression and clinicopathological features remains poorly understood. This study aimed to evaluate these correlations in patients with squamous cell carcinoma of the bronchus, a subgroup that has lagged behind the more prevalent NSCLC subtype—adenocarcinoma—in terms of therapeutic advancements [13, 18].

In our study, 78.7% of patients exhibited PD-L1 positivity (>1%), with 26.6% of these showing high expression levels (>50%). PD-L1 expression below 1% was observed in 21.3% of cases. Similarly, Farrag et al. [21] reported PD-L1 positivity in 71% of patients, with high expression in 59.1% of positive cases. However, Pawelczyk et al. [20] found PD-L1 positivity in only 32.5% of patients with all

NSCLC subtypes, with high expression in 10.6%. This discrepancy may stem from differences in testing methodologies, patient populations, or PD-L1 evaluation criteria. Moreover, interpretation is further complicated by intratumoral and intertumoral heterogeneity, biopsy technique variability, and the use of different immunohistochemistry (IHC) assays for PD-L1 detection [11, 21]. The KEYNOTE-042 study conducted by Reck et al. [22] demonstrated a significant survival benefit in patients with high PD-L1 expression followed over 47 months. Pembrolizumab significantly prolonged overall survival in patients with high PD-L1 expression (TPS ≥50%), while survival in the intermediate-expression group (TPS 1%–49%) appeared similar to chemotherapy [22].

No statistically significant association was found between PD-L1 expression and sex (p=0.845), consistent with findings by Chen et al. (p=0.337) [6]. However, the relationship remains controversial; Pan et al. [23] found high expression (≥50%) significantly associated with male sex (p=0.026), whereas Karatrasoglou et al. [24] reported higher expression rates in females. In light of such divergent findings, a systematic review by Brody et al. [25], encompassing 16 studies, did not identify a statistically significant correlation between PD-L1 expression and sex. Farrag et al. [19] observed no correlation between PD-L1 expression and age (p=0.716), consistent with Brody et al. [25]. In contrast, our study revealed a marginal association (p=0.058).

Regarding other clinicopathological parameters, our findings did not indicate a significant association between PD-L1 expression and tumor laterality or TNM stage. Similarly, Shimoji et al. [26] reported no correlation between PD-L1 expression and TNM stage, whereas Chen et al. [9] identified TNM stage as a significant prognostic factor (p<0.001). A strength of our study lies in its inclusion of patients across all disease stages, providing a broader view compared to previous studies focusing on specific subgroups.

The impact of smoking history on PD-L1 expression has yielded conflicting findings. Three studies identified a significant correlation between high PD-L1 expression (≥50%) and current/former smoking status [23, 27, 28]. Pan et al. [23] reported a significant association in an East Asian population (p=0.008), and similar results were found by Gainor et al. [28] (p<0.001). Our study did not observe a statistically significant association (p=0.323), although 72% of patients with high expression were smokers. Variability in findings may result from differing sample sizes and the reliance on self-reported smoking status, which also represents a limitation of our study. Additionally, the study's retrospective and single-center design may affect generalizability.

Although data suggest a potential association between smoking history and high PD-L1 expression, further prospective and multicenter studies using standardized methodologies are warranted to better evaluate this relationship. It is also known that smoking can impair immune function, further complicating immunotherapy efficacy. Some studies suggest that active smoking during immunotherapy may reduce treatment effectiveness, whereas tobacco-related mutational burden may serve as a predictive biomarker for anti-PD-1 response [29].

The ECOG Performance Status scale assesses overall patient condition by integrating multiple influencing factors. Differentiating between functional decline due to comorbidities versus tumor progression can critically affect prognosis and possibly immunotherapy outcomes. Our study identified the highest proportion of patients in ECOG 1, followed by ECOG 0 and ECOG 2. A significant association was found between ECOG 0 and PD-L1 expression <1%, which may serve as a negative selection criterion for PD-L1 testing. In contrast, Lars Henning Schmidt et al. found no significant association in their squamous NSCLC subgroup (p=0.867) [30], despite also reporting the highest prevalence in ECOG 1 and 2 Lin et al. [31], who studied the adenocarcinoma subtype, also failed to find a statistically significant association. These findings underscore the need for further investigation into the complex relationship between ECOG status and PD-L1 expression across different NSCLC histologies. Due to contradictory evidence regarding the association of clinicopathological characteristics with PD-L1 expression, selecting the ideal patient population for PD-L1 testing remains challenging. Our study observed minimal expression levels among patients with better functional status, suggesting a potential inverse relationship between PD-L1 expression, tumor progression, and patient age.

Further research is necessary to clarify the role of the tumor microenvironment in modulating PD-L1 expression and to determine whether high PD-L1 expression represents a cause, consequence, or merely a correlative marker of tumor progression and functional deterioration.

Conclusion

The prevalence of PD-L1 positivity among patients was 78.7%. Low-level positivity (1–49%) was observed in 52.1% of cases, while high expression (>50%) was found in 26.6% of patients. No statistically significant association was identified between the percentage of PD-L1-positive tumor cells and sex (p=0.845), tumor laterality (p=0.670), smoking status (p=0.323), or TNM stage (p=0.603). A statistically significant association was found between ECOG Performance Status and PD-L1 expression <1% (p=0.035), while a marginal association was observed between PD-L1 expression >50% and patient age (p=0.058). Further studies involving larger patient cohorts are necessary to draw definitive conclusions.

Literature

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70:7–30.
[2] Institut za javno zdravlje Srbije „Dr Milan Jovanović Batut“ (homepage on the Internet). Maligni tumori u Republici Srbiji 2021. 2023. (cited 2024 April 23). Available from: https://www.batut.org.rs/download/publikacije/MaligniTumoriURepubliciSrbiji2021.pdf
[3] Myers R, Brauer M, Dummer T, et al. High-ambient air pollution exposure among never smokers versus ever smokers with lung cancer. J Thorac Oncol. 2021;16:1850-8.
[4] Kumar V, Abbas AK, Aster JC. Robbins & Cotran Pathologic Basis of Disease. 9th ed. Elsevier: Philadelphia; 2015.
[5] Perin B. Nemikrocelularni karcinom bronha (carcinoma bronchiogenes nonmicrocellulare). In: Popović S, Obradović D, editors. Interna medicina I. Novi Sad: Medicinski fakultet Novi Sad; 2022. p.71-83.

[6] Chen Y, Wang L, Zhu H, Li X, Zhu Y, Yin Y, et al. Relationship between programmed seath-ligand 1 and clinicopathological characteristics in non-small cell lung cancer patients. Chin Med J. 2013;28:147–51.
[7] Vallonthaiel AG, Malik PS, Singh V, Kumar V, Kumar S, Sharma MC, et al. Clinicopathologic correlation of programmed death ligand-1 expression in non-small cell lung carcinomas: A report from India. Ann Diagn Pathol. 2017;31:56–61.
[8] Patel SP, Kurzrock R. PD-L1 Expression as a predictive biomarker in cancer immunotherapy. Mol Cancer Ther. 2015;14:847–56.
[9] Chen Y, Mu CY, Huang JA. Clinical significance of programmed death-1 ligand-1 expression in patients with non-small cell lung cancer: A 5-year-follow-up Study. Tumori J. 2012;98:751–5.
[10] Hyojin K, Chung JH. PD-L1 testing in non-small cell lung cancer: past, present, and future. J Pathol Transl Med. 2019;53:199-206.
[11] Gompelmann D, Sarova P, Mosleh B, Papaporfyriou A, Oberndorfer F, Idzko M, et al. PD-L1 assessment in lung cancer biopsies-pitfalls and limitations. Int J Biol Markers. 2024;39:3-8.
[12] Phillips W, Thornton Z, Andrews L, Daly R, Higgins J, Davies P, et al. Efficacy of PD-1/PD-L1 immunotherapy on brain metastatic non-small-cell lung cancer and treatment-related adverse events: A systematic review. Crit Rev Oncol Hematol. 2024;196:104288
[13] Perez-Moreno P, Brambilla E, Thomas R, Soria JC. Squamous cell carcinoma of the lung: molecular subtypes and therapeutic opportunities. Clin Cancer Res. 2012;18:2443-51.
[14] Ullah A, Pulliam S, Karki NR, Khan J, Jogezai S, Sultan S, et al. PD-L1 over-expression varies in different subtypes of lung cancer: will this affect future therapies? Clin Pract. 2022;12:653-71.
[15] Wang L, Hu Y, Wang S, Shen J, Wang X. Biomarkers of immunotherapy in non-small cell lung cancer. Oncol Lett. 2020;20:139.
[16] Onoi K, Chihara Y, Uchino J, Shimamoto T, Morimoto Y, Iwasaku M, et al. Immune checkpoint inhibitors for lung cancer treatment: a review. J Clin Med. 2020;9:1362.
[17] Aguiar Jr PN, Perry LA, Penny-Dimri J, Babiker H, Tadokoro H, de Mello RA. The effect of PD-L1 testing on the cost-effectiveness and economic impact of immune checkpoint inhibitors for the second-line treatment of NSCLC. Ann Oncol. 2017;28:2256-63.
[18] Gandara DR, Hammerman PS, Sos ML, Lara PN Jr, Hirsch Fr. Squamous cell lung cancer: from tumor genomics to cancer therapeutics. Clin Cancer Res. 2015;21:2236–43.
[19] Farrag M, Ibrahim E, Abdelwahab H, Elsergany A, Elhadidy T. PDL-1 expression in lung carcinoma and its correlation with clinicopathological and prognostic characteristics. J Immunoassay Immunochem. 2021;42:679-90.
[20] Pawelczyk K, Piotrowska A, Ciesielska U, Jablonska K, Gletzel-Plucinska N, Grzegrzolka J, et al. Role of PD-L1 expression in non-small cell lung cancer and their prognostic significance according to clinicopathological factors and diagnostic markers. Int. J. Mol. Sci. 2019;20:824.
[21] Caldwell C Jr, Johnson CE, Balaji VN, Balaji GA, Hammer RD, Kannan R. Identification and validation of a PD-L1 binding peptide for determination of PD-L1 expression in tumors. Sci Rep. 2017;7:13682.
[22] Reck M, Remon J, Hellmann MD. First-line immunotherapy for non-small-cell lung cancer. J Clin Oncol. 2022;40:586-97.
[23] Pan Y, Zheng D, Li Y, Cai X, Zheng Z, Jin Y, et al. Unique distribution of programmed death ligand 1 (PD-L1) expression in East Asian non-small cell lung cancer. J Thorac Dis. 2017;9:2579–86.

[24] Karatrasoglou EA, Chatziandreou I, Sakellariou S. Association between PD-L1 expression and driver gene mutations in non-small cell lung cancer patients: correlation with clinical data. Virchows Arch. 2020;477:207–17.
[25] Brody R, Zhang Y, Ballas M, Siddiqui MK, Gupta P, Barker C, et al. PD-L1 expression in advanced NSCLC: Insights into risk stratification and treatment selection from a systematic literature review. Lung Cancer. 2017;112:200-15.
[26] Shimoji M, Shimizu S, Sato K, Suda K, Kobayashi Y, Tomizawa K, et al. Clinical and pathologic features of lung cancer expressing programmed cell death ligand 1 (PD-L1). Lung Can. 2016;98:69–75.
[27] Norum J, Nieder C. Tobacco smoking and cessation and PD-L1 inhibitors in non-small cell lung cancer (NSCLC): a review of the literature. ESMO Open. 2018;3;e000406.
[28] Gainor F, Shaw AT, Sequist LV, Fu X, Azzoli CG, Piotrowska Z, et al. EGFR mutations and ALK rearrangements are associated with low response rates to PD-1 pathway blockade in non-small cell lung cancer: A retrospective analysis. Clin Cancer Res. 2016;22:4585-93.
[29] Bodor JN, Bauman JR, Handorf EA, Ross EA, Clapper ML, Treat J. Real-world progression-free survival (rwPFS) and the impact of PD-L1 and smoking in driver-mutated non-small cell lung cancer (NSCLC) treated with immunotherapy. J Cancer Res Clin Oncol. 2023;149:1755-63.
[30] Schmidt LH, Kümmel A, Görlich D, Mohr M, Bröckling S, Mikesch JH, et al. PD-1 and PD-L1 expression in NSCLC indicate a favorable prognosis in defined subgroups. PLoS One. 2015;10:e0136023.
[31] Lin C, Chen X, Li M, Liu J, Qi X, Yang W, et al. Programmed death-ligand 1 expression predicts tyrosine kinase inhibitor response and better prognosis in a cohort of patients with epidermal growth factor receptor mutation-positive lung adenocarcinoma. Clin Lung Cancer. 2015;16:25-35.

POVEZANOST KLINIČKO−PATOLOŠKIH KARAKTERISTIKA I EKSPRESIJE *PD−L*1 KOD PACIJENATA SA SKVAMOZNIM KARCINOMOM BRONHA

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Sažetak. *Skvamozni karcinom bronha ne reaguje uvek na standardnu onkološku terapiju. Većina aktuelnih istraživanja se bazira na imunoterapiji koja cilja kontrolne tačke ćelijske imunosti. Procena nivoa ekspresije PD-L1 (engl. programmed death-ligand 1 − ligand receptora programirane ćelijske smrti 1) je neophodan preduslov za donošenje odluke o potencijalnom lečenju monoklonskim antitelima inhibitorima PD-1/PD-L1 signalnog puta. Cilj istraživanja je utvrditi povezanost ekspresije PD-L1 kod skvamoznog karcinoma bronha sa kliničko−patološkim karakteristikama poput pola, prosečne starosti, pušačkog statusa, lokalizacija tumora, TNM stadijuma i ECOG Perfomans status skale kod pacijenata lečenih u Institutu za plućne bolesti Vojvodine (IPBV). Retrospektivno ispitivanje je obuhvatilo 94 ispitanika oba pola, u periodu od 1. januara do 31. decembra 2021. godine, kod kojih je na osnovu patohistološke analize dijagnostikovan skvamozni karcinom bronha i odrađena imunohistohemijska*

procena ekspresija PD-L1. Materijal za patohistološku analizu obrađen je u Službi za patoanatomsku i molekularnu dijagnostiku IPBV. Pozitivna PD-L1 ekspresija (>1%) detektovana je kod 78,7% ispitanika, a 52,1% pokazalo je visoku ekspresiju (>50%). Multivarijantnom analizom nije pronađena statistički značajna povezanost procenta pozitivnosti tumorskih ćelija u odnosu na pol (p=0,845), lokalizaciju (p=0,670), pušački status (p=0,323) i TNM stadijuma (p=0,603). Statistički značajna povezanost dokazana je između ECOG Performans Status skale i PD-L1 ekspresije <1% (p=0,035), dok marginalna povezanost postoji između PD-L1 procenta ekspresije >50% i starosti (p=0,058). Ekspresija PD-L1 kod pacijenata sa skvamoznim karcinomom bronha nije jasno povezana sa kliničkim karakteristikama bolesti i patohistološkim nalazom. Starost pacijenata i performans status mogu sugerisati postojanje PD-L1 ekspresije. Druge ispitane kliničko−patološke karakteristike nisu od značajnosti. Dalja istraživanja na većem uzorku pacijenata su neophodna za donošenje adekvatnih zaključaka.

Ključne reči: *Skvamozni karcinom bronha; Ekspresija PD-L1; Prediktivni biomarker; Kliničko−patološke karakteristike*