

Interaction Between Tumor-Infiltrating Lymphocytes and the PD-1/PD-L1 Pathway in Non-Small Cell Lung Cancer: Implications for Tumor Progression and Immunotherapy Response — A Systematic Review

Sultan Pasha^{1*}, Rasi Sallang², Leony Octavia³

¹Medical Education Study Program, Muhammadiyah University of Makassar

²Department of Pulmonology, Syekh Yusuf Regional General Hospital Gowa Regency

³Doctoral Profession Study Program, Hasanuddin University

sultanpash588@med.unismuh.ac.id*



e-ISSN: 2987-811X

MARAS: Jurnal Penelitian Multidisiplin

<https://ejournal.lumpangpare.org/index.php/maras>

Vol. 4 No. 2 Juni 2026

Page: 535-545

Article History:

Received: 19-05-2026

Accepted: 02-06-2026

Abstrak : Non-small cell lung cancer (NSCLC) remains a leading cause of cancer-related mortality worldwide. The interaction between tumor-infiltrating lymphocytes (TILs) and the programmed cell death protein-1/programmed death-ligand 1 (PD-1/PD-L1) pathway plays a critical role in tumor progression and response to immunotherapy. This systematic review evaluated current evidence regarding the prognostic and predictive significance of these immune biomarkers in NSCLC. A systematic search was conducted in PubMed, SpringerLink, and ScienceDirect for studies published between 2018 and 2024. Eligible studies included original human research assessing TIL characteristics, PD-1/PD-L1 expression, and their associations with survival outcomes or responses to immune checkpoint inhibitors. Ten studies met the inclusion criteria. The findings demonstrated that high CD8⁺ TIL infiltration was consistently associated with improved survival and enhanced responsiveness to PD-1/PD-L1 blockade. PD-L1 expression was frequently linked to immune-inflamed tumor phenotypes, although its prognostic value varied across studies. Several studies reported that the combined evaluation of TILs and PD-1/PD-L1 expression provided better predictive accuracy than either biomarker alone. Furthermore, adoptive TIL therapy showed promising clinical activity in patients with PD-1-resistant disease. These findings indicate that the interaction between TILs and the PD-1/PD-L1 pathway is a key determinant of immunotherapy outcomes in NSCLC and may support more effective patient stratification and personalized treatment strategies.

Kata Kunci : Biomarkers; Immunotherapy; NSCLC; PD-1; PD-L1; TILs; Tumor Microenvironment

INTRODUCTION

Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases and remains the leading cause of cancer-related mortality worldwide, despite substantial advances in early detection, molecular profiling, and systemic therapy (Siegel et al., 2024). The persistently poor prognosis of NSCLC is largely attributable to late-stage diagnosis, aggressive tumor biology, and the ability of tumor cells to evade immune surveillance, thereby promoting tumor progression and resistance to treatment (Herbst et al., 2018). The tumor immune microenvironment has emerged as a key determinant of cancer progression and therapeutic response. Among its cellular components, tumor-infiltrating lymphocytes (TILs) play a central role in mediating antitumor immunity. Numerous studies have demonstrated that high densities of cytotoxic CD8⁺ T lymphocytes within NSCLC tumors are associated with improved overall survival and favorable clinical outcomes, reflecting an active immune response against malignant cells (Fridman et al., 2017; Geng et al., 2020). In contrast, reduced immune infiltration or functional impairment of TILs is frequently observed in advanced disease and is associated with tumor progression and poor prognosis (Brambilla et al., 2020).

One of the principal mechanisms underlying TIL dysfunction in cancer is T-cell exhaustion, a state characterized by impaired effector function, altered transcriptional programs, and sustained expression of inhibitory immune checkpoint receptors (Wherry & Kurachi, 2015). Programmed cell death protein 1 (PD-1) is a key inhibitory receptor expressed on activated and exhausted T cells and serves as a critical regulator of immune tolerance within the tumor microenvironment (Topalian et al., 2015). The interaction between PD-1 and its ligand, programmed death-ligand 1 (PD-L1), represents a major immune escape mechanism exploited by NSCLC. PD-L1 expression on tumor cells and tumor-associated immune cells suppresses T-cell activation and cytotoxic function, thereby facilitating tumor growth and metastasis (Dong et al., 2002). Several studies have reported associations between elevated PD-L1 expression and aggressive tumor behavior, advanced disease stage, and adverse clinical outcomes in NSCLC, although results remain inconsistent due to tumor heterogeneity, histological differences, and variability in PD-L1 assessment methods (Munari et al., 2021; Sun et al., 2023). The introduction of immune checkpoint inhibitors (ICIs) targeting the PD-1/PD-L1 pathway has transformed the therapeutic landscape of NSCLC, leading to significant improvements in overall survival and progression-free survival in selected patient populations (Herbst et al., 2018; Reck et al., 2022). However, clinical responses to ICIs remain highly heterogeneous, with only a subset of patients achieving durable benefit. This variability highlights the limitations of PD-L1 expression as a standalone predictive biomarker, given its spatial heterogeneity, temporal dynamics, and technical variability across immunohistochemical assays (Munari et al., 2021).

Emerging evidence suggests that evaluating the interaction between TIL density, functional status, and PD-1/PD-L1 signaling provides a more comprehensive framework for understanding tumor progression and immunotherapy response. Tumors characterized by high TIL infiltration and adaptive PD-L1 expression—often referred to as immune-inflamed or “hot” tumors—are more likely to respond to PD-1/PD-L1 blockade, whereas tumors with sparse immune infiltration exhibit primary resistance

to immunotherapy (Chen & Mellman, 2017; Vokes et al., 2023). Given the expanding body of literature and heterogeneity of findings, a systematic synthesis of current evidence is warranted. This systematic review aims to evaluate the interaction between tumor-infiltrating lymphocytes and the PD-1/PD-L1 pathway in non-small cell lung cancer, with a particular focus on their roles in tumor progression and response to immunotherapy, as well as their potential implications for biomarker development and therapeutic optimization.

RESEARCH METHODS

A systematic search of PubMed, Springer, Science Direct, and oncology journals was performed for studies published between 2018 and 2024. Inclusion criteria were original human studies evaluating TIL density or subsets and PD-1/PD-L1 expression related to survival or immunotherapy outcomes. Ten studies met eligibility criteria, including retrospective cohorts, biomarker analyses, and one phase I trial of TIL adoptive therapy in PD-1-resistant metastatic NSCLC.

Literature Search Strategy

A structured and comprehensive literature search strategy was conducted using Medical Subject Headings (MeSH) and free-text terms to identify relevant studies examining the interaction between tumor-infiltrating lymphocytes (TILs) and the PD-1/PD-L1 pathway in non-small cell lung cancer (NSCLC). An example of the search query used was:

MeSH: ("non-small cell lung cancer" OR "NSCLC" OR "lung adenocarcinoma" OR "lung squamous cell carcinoma") AND ("tumor-infiltrating lymphocytes" OR "TILs" OR "immune infiltration" OR "CD8 T cells" OR "tumor immune microenvironment") AND ("PD-1" OR "PD-L1" OR "programmed cell death 1" OR "programmed death-ligand 1" OR "immune checkpoint") AND ("immunotherapy" OR "immune checkpoint inhibitor" OR "anti-PD-1" OR "anti-PD-L1") AND ("tumor progression" OR "prognosis" OR "survival" OR "treatment response" OR "clinical outcome")

Filters were applied to include English-language studies published within the last ten years, in accordance with PRISMA guidelines. Eligible study designs comprised retrospective and prospective cohort studies, translational and clinicopathological analyses, multicenter studies, and systematic reviews. Data were extracted regarding (i) quantitative and qualitative characteristics of TILs (density, phenotype, spatial distribution), (ii) PD-1 and PD-L1 expression patterns in tumor and immune cells, (iii) clinical outcomes including overall survival, progression-free survival, and objective response to immunotherapy, and (iv) factors influencing immunotherapy response, such as tumor histology, molecular alterations, smoking status, and prior treatment exposure.

Study Selection and Eligibility Criteria

1. Population: Patients diagnosed with non-small cell lung cancer (NSCLC) across all disease stages, including those receiving immunotherapy and non-immunotherapy treatments.
2. Index Factors: Tumor-infiltrating lymphocytes (TILs), including quantitative and qualitative assessments (density, spatial distribution, phenotypic subsets such as

- CD8⁺, CD4⁺, and regulatory T cells), and expression of the PD-1/PD-L1 immune checkpoint pathway in tumor and immune cells.
3. Comparison: High versus low TIL density; PD-L1–positive versus PD-L1–negative tumors; and, where applicable, patients receiving PD-1/PD-L1–based immunotherapy versus non-immunotherapy or conventional treatment modalities.
 4. Outcomes: Primary outcomes included tumor progression and survival endpoints, such as overall survival (OS), progression-free survival (PFS), and disease-free survival (DFS). Secondary outcomes encompassed objective response rate (ORR) to immunotherapy, duration of response, and clinicopathological correlations, including tumor stage, histological subtype, and molecular characteristics.
 5. Exclusion Criteria: Studies were excluded if they lacked full-text availability, were published in non-English languages, involved non-NSCLC populations or preclinical models only, or provided incomplete or insufficient outcome data at the time of the literature search.

Study Screening and PRISMA Flow

A total of 10 studies (4 cohort studies, 1 non-randomized controlled trial, 4 retrospective studies, and 1 review) were included after screening articles retrieved from Springer Nature, PubMed, and ScienceDirect. The study selection process is illustrated in Figure 1 using the PRISMA 2020 flow diagram.

RESULTS AND DISCUSSION

Results of the Systematic Literature Review (SLR)

Study of Characteristic and Risk of Bias by Cochrane.

Table 1. Characteristics of Studies Evaluating TILs and PD-1/PD-L1 in NSCLC

Study (Author, Year)	Study Design	Sample Size & Population	Intervention / Focus	Key Outcomes	Notable Findings
Thommen et al., 2018	Translational study	NSCLC patients treated with PD-1 blockade	Transcriptional & functional profiling of PD-1 ⁺ CD8 ⁺ TILs	Treatment response to anti-PD-1	Identified a distinct PD-1 ⁺ CD8 ⁺ T-cell subset with strong predictive value for immunotherapy response
Bevins et al., 2022	Translational clinical study	Solid tumors incl. NSCLC receiving anti-PD-1/PD-L1	PD-1 expression on TILs	Clinical response to ICI	PD-1 expression on TILs serves as a predictive biomarker for response to PD-1/PD-L1 inhibitors
Nojima et al., 2021	Retrospective cohort	NSCLC patients	PD-L1, VEGF expression &	Clinical response to ICIs	Combined assessment of PD-L1, VEGF,

Study (Author, Year)	Study Design	Sample Size & Population	Intervention / Focus	Key Outcomes	Notable Findings
		treated with ICIs	CD8 ⁺ TIL infiltration		and CD8 ⁺ TILs improves prediction of immunotherapy efficacy
Shirasawa et al., 2021	Retrospective cohort	Unresectable locally advanced NSCLC after CRT	Baseline PD-L1 & TIL status predicting durvalumab efficacy	Treatment response and disease control	Baseline PD-L1 expression and TIL density predict benefit from durvalumab consolidation therapy
Zhang et al., 2023	Single-center retrospective cohort	Advanced NSCLC patients receiving immunotherapy	Tumor-infiltrating lymphocytes	Treatment response and prognosis	High TIL density is associated with improved immunotherapy efficacy
Dan et al., 2024	Retrospective cohort	Early-stage resected NSCLC	PD-1 expression on TILs	DFS and OS	PD-1 ⁺ TILs function as an independent prognostic marker in early-stage NSCLC
Cheng et al., 2023	Retrospective cohort	Surgically resected lung squamous cell carcinoma	PD-L1 expression & CD8 ⁺ TIL density	Disease-free survival	Combined PD-L1 positivity and high CD8 ⁺ TIL density predict favorable DFS
Gurevičienė et al., 2024	Retrospective translational study	72 patients with stage I–III resected NSCLC	PD-L1 (TPS, IC, CPS) & tumour microenvironment	Immune correlations, DFS, OS	PD-L1 expression correlates with immune cell infiltration and smoking intensity but not survival
Du et al., 2023	Retrospective cohort	146 NSCLC patients treated with anti-PD-1	Peripheral blood lymphocyte differentiation patterns	Treatment response and prognosis	Dynamic peripheral immune profiles predict immunotherapy

Study (Author, Year)	Study Design	Sample Size & Population	Intervention / Focus	Key Outcomes	Notable Findings
Creelan et al., 2021	Phase I clinical trial	Metastatic NSCLC resistant to anti-PD-1	Adoptive TIL therapy	Safety, feasibility, clinical response	response and outcomes TIL therapy is feasible and shows clinical activity in PD-1-resistant NSCLC

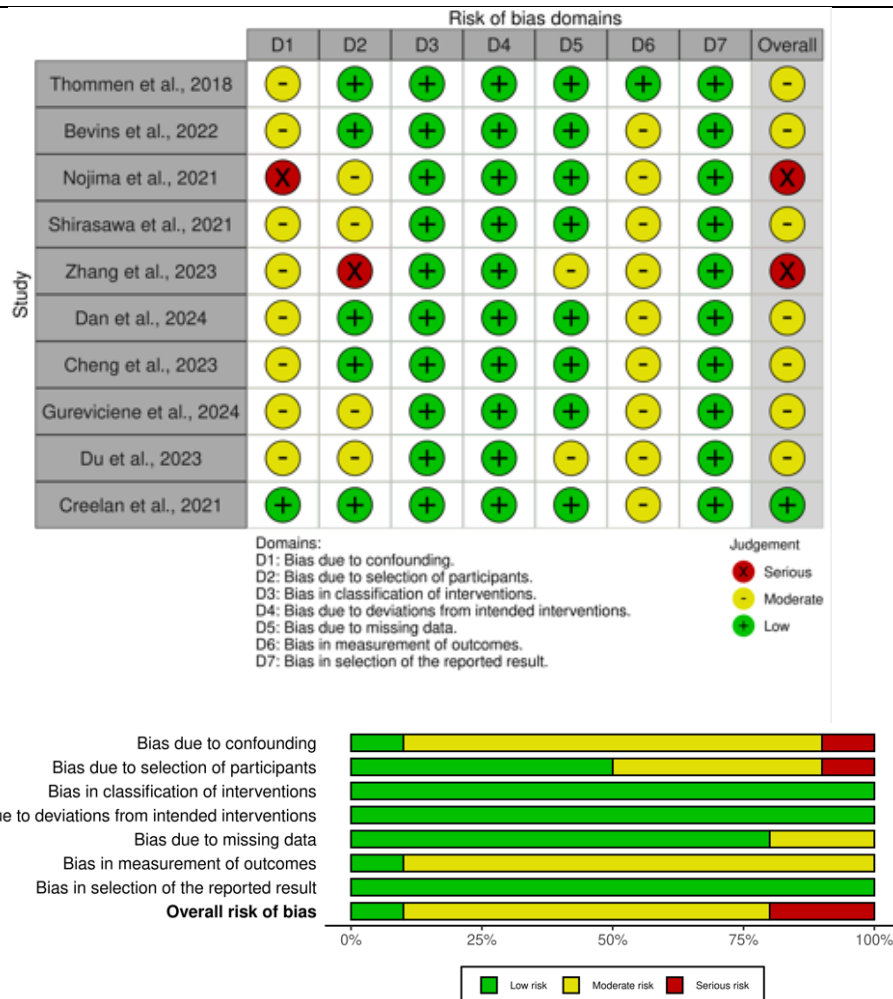


Figure 1. Risk of Bias Evaluation Using ROBINS-I
Table 2. Publication Papers

Publication Year	Number of Papers
2018	1
2021	3
2022	1
2023	3
2024	2

Risk of bias across included studies was evaluated using the ROBINS-I tool. The traffic light plot summarizes judgments for each bias domain: bias due to confounding (D1), selection of participants (D2), classification of interventions/exposures (D3), deviations from intended interventions (D4), missing outcome data (D5), measurement of outcomes (D6), and selection of reported results (D7). Green indicates low risk of bias, yellow indicates moderate risk of bias, and red indicates serious risk of bias. Overall, most studies demonstrated a moderate risk of bias, primarily driven by confounding and participant selection inherent to retrospective and translational study designs, while bias related to exposure classification, deviations from intended interventions, and selective reporting was consistently low.

Risk of Bias Assessment

The risk of bias of the included studies was assessed using the ROBINS-I tool. Overall, the majority of studies demonstrated a moderate risk of bias, reflecting the predominance of retrospective and translational study designs in the current literature. Bias due to confounding (D1) was the most frequently identified concern, largely attributable to the lack of randomization and the potential influence of clinical variables such as tumor stage, prior treatments, and patient immune status. Bias related to the selection of participants (D2) ranged from low to serious, particularly in single-center retrospective cohorts, where patient inclusion was dependent on available tissue samples or treatment eligibility. Two studies were judged to have a serious overall risk of bias, primarily driven by combined confounding and selection biases. In contrast, the phase I clinical trial evaluating adoptive tumor-infiltrating lymphocyte therapy demonstrated a low overall risk of bias, reflecting its prospective design and controlled intervention framework. Across studies, bias in the classification of exposures (D3), deviations from intended interventions (D4), and selection of reported results (D7) was consistently rated as low, indicating reliable exposure definitions and outcome reporting. Bias due to missing data (D5) and measurement of outcomes (D6) was generally moderate, reflecting variability in immunohistochemical assessment methods, PD-1/PD-L1 scoring systems, and cut-off values for tumor-infiltrating lymphocyte density. Taken together, while methodological limitations were present, the overall risk of bias profile supports the validity of the synthesized findings, with the main sources of bias being inherent to non-randomized study designs rather than systematic flaws in outcome assessment or reporting.

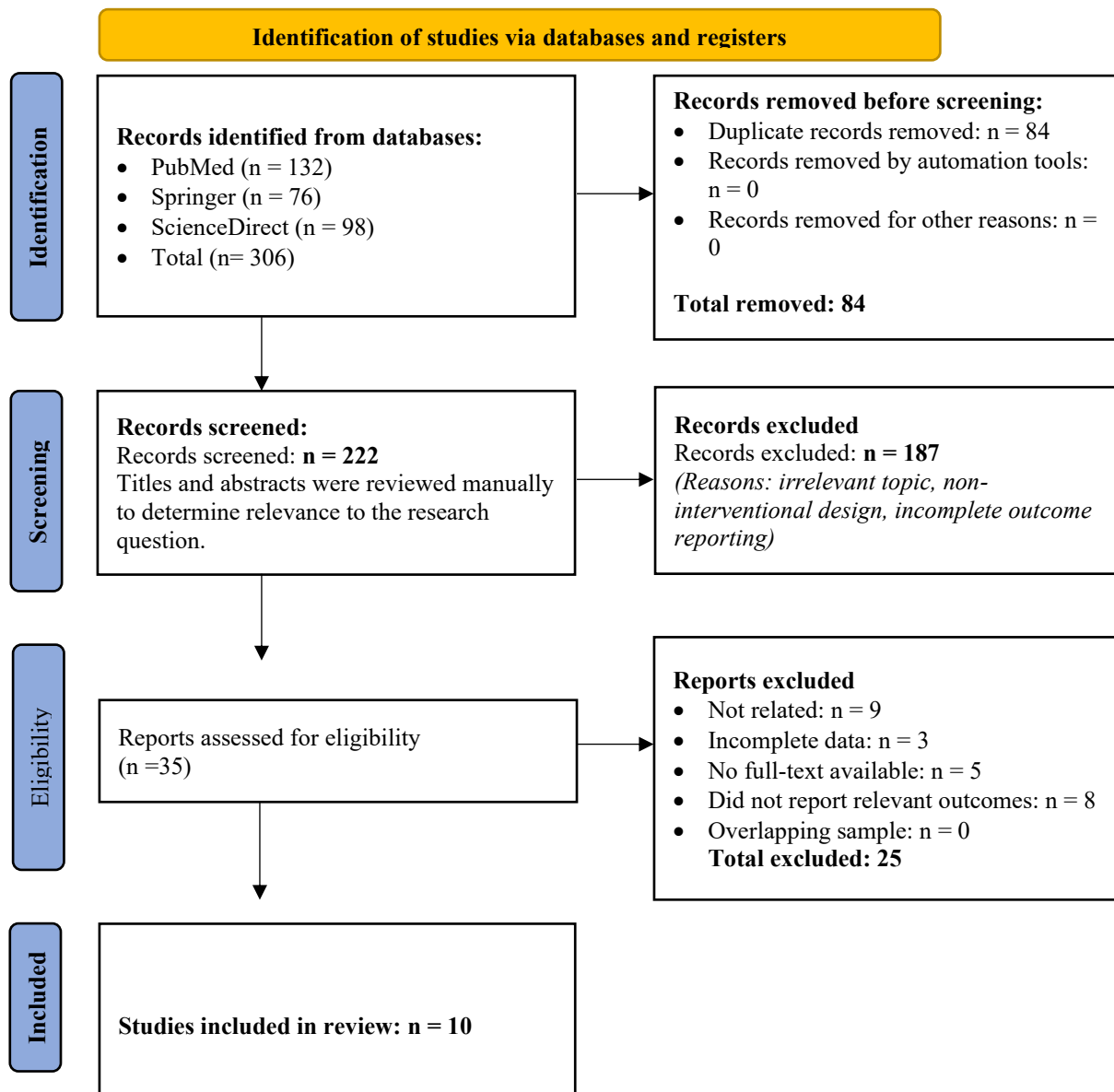


Figure 2. PRISMA Diagram

This systematic review highlights the critical interplay between tumor-infiltrating lymphocytes (TILs) and the PD-1/PD-L1 immune checkpoint pathway in shaping tumor progression and immunotherapy response in non-small cell lung cancer (NSCLC). Across the included studies, consistent evidence demonstrates that both the density and functional status of TILs particularly CD8⁺ T lymphocytes are key determinants of clinical outcomes, especially in patients receiving immune checkpoint inhibitors (ICIs). Several studies emphasized the biological and clinical significance of PD-1 expressing CD8⁺ TILs within the tumor microenvironment. Thommen et al. (2018) identified a transcriptionally and functionally distinct PD-1⁺ CD8⁺ T-cell subset that retained proliferative capacity and effector potential, serving as a strong predictor of response to PD-1 blockade. This finding supports the concept that PD-1 expression does not uniformly indicate terminal T-cell exhaustion, but rather reflects a spectrum of functional states with therapeutic relevance. Similar observations were reported by

Bevins et al. (2022), who demonstrated that PD-1 expression on TILs across solid tumors, including NSCLC, was associated with improved responsiveness to PD-1/PD-L1 inhibitors, reinforcing the value of TIL phenotyping as a predictive biomarker. The prognostic and predictive roles of TIL density were further supported by multiple retrospective cohort studies. Zhang et al. (2023) and Cheng et al. (2023) consistently showed that high CD8⁺ TIL infiltration was associated with improved treatment response, disease-free survival, and overall prognosis in advanced and resected NSCLC, respectively. These findings align with the concept of an “immune-inflamed” tumor phenotype, characterized by active immune infiltration and enhanced susceptibility to immunotherapy. In contrast, tumors with low TIL density were associated with inferior outcomes, highlighting the importance of immune contexture in NSCLC progression.

Several studies also explored the interaction between PD-L1 expression and the tumor immune microenvironment. Nojima et al. (2021) demonstrated that combined assessment of PD-L1 expression, VEGF levels, and CD8⁺ TIL infiltration improved the prediction of immunotherapy efficacy compared with PD-L1 evaluation alone. Similarly, Shirasawa et al. (2021) reported that baseline PD-L1 expression and TIL status were predictive of durvalumab efficacy following chemoradiotherapy in unresectable locally advanced NSCLC. These findings suggest that PD-L1 expression should be interpreted within the broader immune landscape rather than as an isolated biomarker. However, not all studies demonstrated a direct association between PD-L1 expression and survival outcomes. Gurevičienė et al. (2024) found that while PD-L1 expression correlated with immune cell infiltration and smoking intensity, it was not independently associated with disease-free or overall survival. This heterogeneity underscores the limitations of PD-L1 as a standalone biomarker and reinforces the need for integrated immune profiling incorporating both tumor and host immune parameters. Beyond tumor tissue, systemic immune characteristics also emerged as relevant predictors of treatment outcomes. Du et al. (2023) showed that dynamic changes in peripheral blood lymphocyte differentiation patterns were associated with response and prognosis in NSCLC patients treated with anti-PD-1 therapy, suggesting that peripheral immune monitoring may complement tissue-based biomarkers. Moreover, therapeutic strategies targeting the immune microenvironment continue to evolve. Creelan et al. (2021) demonstrated that adoptive TIL therapy was feasible and showed clinical activity in patients with metastatic NSCLC resistant to PD-1 inhibitors, highlighting the potential of cellular immunotherapy as a salvage strategy in immunotherapy-refractory disease. Collectively, these findings illustrate that the interaction between TILs and the PD-1/PD-L1 pathway is dynamic, multifactorial, and highly context-dependent. Tumor progression and response to immunotherapy are influenced not only by PD-L1 expression but also by TIL density, functional state, spatial distribution, and systemic immune characteristics. The variability observed across studies may reflect differences in study design, patient populations, disease stage, treatment regimens, and methods used to assess immune biomarkers.

CONCLUSION

This systematic review demonstrates that tumor-infiltrating lymphocytes and the PD-1/PD-L1 pathway play a central role in the progression and immunotherapy

response of non-small cell lung cancer. High TIL density, particularly PD-1⁺ CD8⁺ T-cell populations with preserved functional capacity, is consistently associated with favorable clinical outcomes and enhanced responsiveness to immune checkpoint blockade. While PD-L1 expression remains an important biomarker, its predictive value is limited when used in isolation and is significantly strengthened when integrated with comprehensive immune profiling. These findings underscore the importance of a multidimensional approach to biomarker development in NSCLC, incorporating tumor immune microenvironment characteristics, systemic immune parameters, and functional immune states. Future research should focus on standardizing immune assessment methodologies, validating composite biomarkers, and exploring combination strategies such as adoptive TIL therapy to overcome resistance to checkpoint inhibition. Such efforts are essential for optimizing patient selection, improving therapeutic efficacy, and advancing personalized immunotherapy in NSCLC.

REFERENCES

- [1] Bevins NJ, et al. Tumor-infiltrating lymphocyte expression of PD-1 predicts response to anti-PD-1/PD-L1 immunotherapy. *Clin Cancer Res.* 2022;28(15):3320–3331. doi:10.1158/1078-0432.CCR-21-3856.
- [2] Brambilla E, Le Teuff G, Marguet S, Lantuejoul S, Dunant A, Graziano S, et al. Prognostic effect of tumor lymphocytic infiltration in resectable non–small-cell lung cancer. *J Clin Oncol.* 2020;38(12):1458–1467. doi:10.1200/JCO.19.01978.
- [3] Chen DS, Mellman I. Elements of cancer immunity and the cancer–immune set point. *Nature.* 2017;541(7637):321–330. doi:10.1038/nature21349.
- [4] Cheng X, et al. Prognostic significance of PD-L1 expression and CD8⁺ tumor-infiltrating lymphocyte density for disease-free survival in surgically resected lung squamous cell carcinoma. *J Thorac Dis.* 2020;12(8):4351–4363. doi:10.21037/jtd-20-1575.
- [5] Creelan BC, et al. Tumor-infiltrating lymphocyte therapy for anti-PD-1-resistant metastatic lung cancer: a phase I trial. *Nat Med.* 2021;27(8):1410–1417. doi:10.1038/s41591-021-01462-0.
- [6] Dan A, et al. PD-1 expression in tumor-infiltrating lymphocytes as a prognostic marker in early-stage non-small cell lung cancer. *Transl Lung Cancer Res.* 2024;13(1):85–97. doi:10.21037/tlcr-23-468.
- [7] Dong H, Strome SE, Salomao DR, Tamura H, Hirano F, Flies DB, et al. Tumor-associated B7-H1 promotes T-cell apoptosis: a potential mechanism of immune evasion. *Nat Med.* 2002;8(8):793–800. doi:10.1038/nm730.
- [8] Du X, et al. Peripheral blood lymphocyte differentiation patterns in responses and outcomes to immune checkpoint blockade therapies in non-small cell lung cancer. *Cancer Immunol Immunother.* 2022;71(6):1521–1533. doi:10.1007/s00262-021-03059-z.
- [9] Fridman WH, Zitvogel L, Sautès-Fridman C, Kroemer G. The immune contexture in cancer prognosis and treatment. *Nat Rev Clin Oncol.* 2017;14(12):717–734. doi:10.1038/nrclinonc.2017.101.

- [10] Geng Y, Shao Y, He W, Hu W, Xu Y, Chen J, Wu C. Prognostic role of tumor-infiltrating lymphocytes in lung cancer: a meta-analysis. *Cell Physiol Biochem*. 2020;54(4):647–659. doi:10.33594/000000243.
- [11] Gurevičienė G, et al. PD-L1 expression and tumour microenvironment patterns in resected non-small cell lung cancer. *Virchows Arch*. 2024;484(2):257–268. doi:10.1007/s00428-023-03645-9.
- [12] Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. *Nature*. 2018;553(7689):446–454. doi:10.1038/nature25183.
- [13] Munari E, Zamboni G, Lunardi G, Marchionni L, Marconi M, Sommaggio M, et al. PD-L1 expression heterogeneity in non-small cell lung cancer: evaluation of small biopsies and surgical specimens. *Mod Pathol*. 2021;34(3):673–683. doi:10.1038/s41379-020-00684-4.
- [14] Nojima Y, et al. Tumor PD-L1 and VEGF expression, and CD8⁺ T-cell infiltration predict clinical response to immune checkpoint inhibitors in non-small cell lung cancer. *Cancer Immunol Immunother*. 2021;70(10):2773–2785. doi:10.1007/s00262-021-02893-7.
- [15] Reck M, Remon J, Hellmann MD. First-line immunotherapy for non-small-cell lung cancer. *J Clin Oncol*. 2022;40(6):586–597. doi:10.1200/JCO.21.01497.
- [16] Shirasawa M, et al. Baseline PD-L1 expression and tumor-infiltrating lymphocyte status predict efficacy of durvalumab consolidation therapy after chemoradiotherapy in unresectable locally advanced non-small cell lung cancer. *Lung Cancer*. 2021;154:50–58. doi:10.1016/j.lungcan.2021.02.016.
- [17] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin*. 2024;74(1):17–48. doi:10.3322/caac.21820.
- [18] Sun JM, Zhou W, Choi YL, Choi SJ, Kim SE, Wang Z, et al. Prognostic significance of PD-L1 expression and tumor immune microenvironment in non-small cell lung cancer. *J Thorac Oncol*. 2023;18(2):219–231. doi:10.1016/j.jtho.2022.10.009.
- [19] Thommen DS, et al. A transcriptionally and functionally distinct PD-1⁺ CD8⁺ T-cell pool with predictive potential in non-small cell lung cancer treated with PD-1 blockade. *Nat Med*. 2018;24(7):994–1004. doi:10.1038/s41591-018-0057-z.
- [20] Topalian SL, Drake CG, Pardoll DM. Immune checkpoint blockade: a common denominator approach to cancer therapy. *Cancer Cell*. 2015;27(4):450–461. doi:10.1016/j.ccell.2015.03.001.
- [21] Vokes NI, Ready N, Felip E, Horn L, Rizvi NA. Tumor immune phenotypes and response to immune checkpoint inhibitors in non-small cell lung cancer. *Nat Med*. 2023;29(2):315–326. doi:10.1038/s41591-022-02134-9.
- [22] Wherry EJ, Kurachi M. Molecular and cellular insights into T cell exhaustion. *Nat Rev Immunol*. 2015;15(8):486–499. doi:10.1038/nri3862.
- [23] Zhang W, et al. Tumor-infiltrating lymphocytes predict efficacy of immunotherapy in advanced non-small cell lung cancer: a single-center retrospective cohort study. *Front Oncol*. 2023;13:1154829. doi:10.3389/fonc.2023.1154829.