Research Article / *Araştırma Makalesi*

Ege Journal of Medicine / *Ege Tıp Dergisi* 2026; 65 (1): 131-138

Hemoglobin-to-red cell distribution width ratio as a practical prognostic tool in second-line immunotherapy for non–small cell lung cancer

Küçük hücre dışı akciğer kanserinde ikinci basamak immünoterapide hemoglobin–eritrosit dağılım genişliği oranının pratik bir prognostik belirteç olarak değeri

Gökhan Şahin Caner Acar Salih Tünbekici Haydar Çağatay Yüksel Pınar Açar Pınar Gürsoy

Ege University, Faculty of Medicine, Department of Medical Oncology, Izmir/Türkiye

ABSTRACT

Aim: To evaluate the prognostic value of baseline hemoglobin-to–red cell distribution width ratio (HRR) for progression-free survival (PFS) and overall survival (OS) in patients with advanced or metastatic non–small cell lung cancer (NSCLC) receiving second-line nivolumab.

Materials and Methods: Patients with advanced or metastatic NSCLC treated with second-line nivolumab were retrospectively analyzed. Baseline hemoglobin (g/dL) and RDW (%) were obtained prior to treatment initiation, and HRR (Hb/RDW) was calculated. Patients were categorized into low (<0.7) and high (≥0.7) HRR groups using a predefined cutoff. Survival outcomes were assessed using the Kaplan–Meier method, and prognostic factors were evaluated using Cox proportional hazards regression models.

Results: A total of 114 patients were included. Median baseline hemoglobin, RDW, and HRR were 11.2 g/dL, 15.4%, and 0.74, respectively; 57.9% of patients had low HRR. Median PFS was 4.0 months, and patients with high HRR had significantly longer PFS than those with low HRR (6.5 vs 3.2 months; p=0.011). In multivariate analysis, ECOG performance status ≥2, ≥3 metastatic sites, and low HRR independently predicted shorter PFS (low HRR: HR=2.00; p=0.007). Median OS was 10.0 months, with significantly longer OS observed in the high HRR group (18.7 vs 6.0 months; p<0.001). Low HRR remained an independent adverse prognostic factor for OS (HR=2.87; p<0.001).

Conclusion: Baseline HRR is a simple, inexpensive, and independent prognostic marker associated with inferior survival outcomes in advanced or metastatic NSCLC patients treated with second-line nivolumab.

Keywords: Non-small-cell lung, nivolumab, ımmunotherapy, prognosis, hemoglobin/RDW ratio

ÖZ

Amaç: *İkinci basamak nivolumab alan metastatik küçük hücreli dışı akciğer kanseri (KHDAK) hastalarında, tedavi öncesi hemoglobin/kırmızı hücre dağılım genişliği oranının (HRR) progresyonsuz sağkalım (PFS) ve genel sağkalım (OS) üzerindeki prognostik değerini değerlendirmek.*

Gereç ve Yöntem: *Metastatik KHDAK tanılı ve ikinci basamak nivolumab tedavisi alan hastalar retrospektif olarak incelendi. Hemoglobin (g/dL) ve RDW (%) tedavi başlangıcından önce ölçülerek HRR (Hb/RDW) hesaplandı. Önceden tanımlı eşik değere göre hastalar düşük HRR (<0,7) ve yüksek HRR (≥0,7) gruplarına ayrıldı. PFS ve OS Kaplan–Meier yöntemiyle analiz edildi; prognostik faktörler Cox regresyon modelleri ile değerlendirildi.*

Corresponding author: Gökhan Şahin
Ege University, Faculty of Medicine, Department of Medical Oncology, Izmir/Türkiye
E-mail: *gokhan.sahin@ege.edu.tr*
Application date: 29.12.2025 Accepted: 03.01.2026

Bulgular: *Toplam 114 hasta analize dahil edildi. Medyan hemoglobin, RDW ve HRR sırasıyla 11,2 g/dL, %15,4 ve 0,74 idi. Hastaların %57,9'u düşük HRR grubundaydı. Medyan PFS 4,0 ay olup, yüksek HRR grubunda PFS anlamlı olarak daha uzundu (6,5 vs 3,2 ay; p=0,011). Çok değişkenli analizde ECOG performans durumu ≥2, ≥3 metastatik odak ve düşük HRR, daha kısa PFS ile bağımsız olarak ilişkiliydi (HRR: HR=2,00; p=0,007). Medyan OS 10,0 ay olup, yüksek HRR grubunda OS belirgin olarak daha uzundu (18,7 vs 6,0 ay; p<0,001). Düşük HRR, OS için bağımsız kötü prognostik faktör olarak saptandı (HR=2,87; p<0,001).*

Sonuç: *Tedavi öncesi düşük HRR, ikinci basamak nivolumab alan ileri/metastatik KHDAK hastalarında daha kötü sağkalım ile ilişkili, pratik ve düşük maliyetli bir prognostik belirteçtir.*

Anahtar Sözcükler: *Küçük hücreli dışı akciğer kanseri, nivolumab, immünoterapi, prognoz, hemoglobin/RDW oranı*

INTRODUCTION

Lung cancer remains the leading cause of cancer-related mortality worldwide, with an estimated 2.2–2.5 million new cases and 1.8 million deaths annually (1). Non-small cell lung cancer (NSCLC), which includes histological subtypes such adenocarcinoma, squamous cell carcinoma, and large cell carcinoma, accounts for about 80–85% of lung cancer cases (2, 3). Over the past decade, immune checkpoint inhibitors (ICIs) have fundamentally transformed the therapeutic landscape of advanced NSCLC. Nivolumab, a programmed death-1 (PD-1) inhibitor, was approved in 2015 as second-line therapy after platinum-based chemotherapy based on the CheckMate 017 and 057 trials, which demonstrated superior overall survival and a more favorable safety profile compared with docetaxel (4, 5). Similar benefits were observed with pembrolizumab (KEYNOTE-010) and atezolizumab (OAK), establishing ICIs as the standard of care in the second-line setting for both squamous and non-squamous NSCLC (6, 7). However, over 70% of patients eventually experience primary or acquired resistance, highlighting the necessity of accurate prognostic and predictive biomarkers (8).

Currently available biomarkers for immunotherapy selection have notable limitations. Tumor PD-L1 expression, the most widely used biomarker, is associated with improved response rates in patients with high expression levels; however, responses can still occur in PD-L1–negative tumors, and assay variability and intratumoral heterogeneity limit its reproducibility (9, 10). Tumor mutational burden (TMB) has also shown promise but is constrained by the need for next-generation sequencing, high costs, and the lack of standardized cut-off values (11). In parallel, peripheral blood-derived systemic inflammatory markers have become widely available prognostic indicators. Although uneven thresholds and insufficient prospective validation have limited their normal clinical usage, elevated neutrophil-to-lymphocyte ratio (NLR) and composite indices like the Lung Immune Prognostic Index have been linked to worse outcomes in patients receiving ICIs (12, 13). Thus, there remains an unmet need for simple, cost-effective, and widely available biomarkers to refine prognostication in immunotherapy-treated NSCLC.

The hemoglobin-to–red cell distribution width ratio (HRR), calculated from standard complete blood count parameters, reflects both inflammatory and nutritional status and has recently attracted attention as a prognostic marker (14). A 2022 systematic review and meta-analysis including approximately 3,000 cancer patients reported that lower HRR was significantly associated with increased mortality and faster disease progression across multiple malignancies (15). Despite its practicality and low cost, the prognostic value of HRR has not been well defined in NSCLC, particularly in the context of second-line immunotherapy. Therefore, this study aimed to evaluate the prognostic significance of baseline HRR in patients with advanced or metastatic NSCLC treated with second-line nivolumab, hypothesizing that lower HRR would be associated with inferior survival outcomes.

MATERIALS and METHODS

Study design and population

This retrospective study was conducted at the Department of Medical Oncology, Ege University, İzmir, Turkey. The study included patients with advanced or metastatic non–small cell lung cancer (NSCLC) who received nivolumab as a second-line therapy between January 2019 and December 2024. Eligible patients had histologically confirmed NSCLC and had completed at least one cycle of nivolumab.

Patients with incomplete clinical or laboratory data, prior exposure to immune checkpoint inhibitors, or concomitant malignancies were excluded from the analysis. The study protocol was reviewed and approved by the Ege University Medical Research Ethics Committee (Decision No: 25-12T/4, December 4, 2025).

Data collection and laboratory assessment

Clinical data including age, sex, ECOG performance status, histologic subtype, PD-L1 expression, number and sites of metastasis, and treatment outcomes were collected from electronic medical records. Laboratory values were obtained from peripheral blood samples collected within two weeks prior to the first nivolumab infusion. Haemoglobin (Hb) and RDW values were recorded from complete blood count analyses performed using standardized automated hematology analyzers.

Definition of HRR and clinical endpoints

The hemoglobin-to–red cell distribution width ratio (HRR) was calculated by dividing hemoglobin (g/dL) by RDW (%). Based on a predefined cutoff value of 0.7, which was previously reported to have prognostic significance in nivolumab-treated solid tumor cohorts (16), patients were categorized into two groups: low HRR (<0.7) and high HRR (≥0.7).

Progression-free survival (PFS) was defined as the time from initiation of nivolumab to radiological or clinical disease progression or death from any cause, whichever occurred first. Overall survival (OS) was defined as the time from treatment initiation to death from any cause or last follow-up.

Statistical analysis

Continuous variables were expressed as median values with interquartile ranges (IQR), and categorical variables as frequencies and percentages. Group comparisons were performed using the chi-square or Mann–Whitney U test, as appropriate. Survival outcomes were estimated using the Kaplan–Meier method, and differences between groups were assessed using the log-rank test. Univariate and multivariate Cox proportional hazards regression models were applied to identify prognostic factors associated with PFS and OS. Variables with a p value <0.10 in univariate analysis were included in the multivariate model. Statistical analyses were performed using SPSS software, version 28.0.1.1 (IBM Corp., Armonk, NY, USA), and a two-sided p value <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 114 patients who received nivolumab were included in the analysis. The median age was 64.8 years (IQR 59.8–69.9), and most patients were male (79.8%) with an ECOG performance status of 0–1 (77.2%). Adenocarcinoma was the predominant histologic subtype (48.2%). PD-L1 expression was negative in 32.5%, 1–49% in 14.0%, and ≥50% in 24.6% of patients

At treatment initiation, the median hemoglobin, RDW, and HRR values were 11.2 g/dL, 15.4%, and 0.74 (0.57–0.85), respectively. According to the predefined cut-off, 66 patients (57.9%) were classified as the low HRR group (<0.7), and 48 (42.1%) as the high HRR group (≥0.7). The median NLR was 3.8 (IQR 1.9–5.6). Brain metastasis was present in 21.1% of patients, and 57.9% had ≥3 metastatic sites at baseline. Baseline characteristics of the study population are summarized in Table-1.

Prognostic significance of hemoglobin-to-RDW ratio for PFS

PFS for the entire cohort was 4.0 months (95% CI, 3.1–4.9). Patients with a high hemoglobin-to-RDW ratio (HRR ≥ 0.7) had significantly longer PFS compared with those with a low HRR (< 0.7) (median, 6.5 months [95% CI, 3.6–9.4] vs. 3.2 months [95% CI, 2.7–3.7]; p = 0.011; Figure-1).

In the univariate analysis, poor ECOG performance status (≥ 2; HR = 2.94, 95% CI 1.83–4.71; p < 0.001), presence of ≥ 3 metastatic sites (HR = 1.76, 95% CI 1.16–2.67; p = 0.007), and low HRR (HR = 1.68, 95% CI 1.21–2.53; p = 0.012) were significantly associated with shorter PFS. In the multivariate model, ECOG performance status ≥ 2 (HR = 2.71, 95% CI 1.48–4.96; p = 0.010), ≥ 3 metastatic sites (HR = 1.73, 95% CI 1.01–2.98; p = 0.047), and low HRR (HR = 2.00, 95% CI 1.21–3.30; p = 0.007) remained independent predictors of inferior PFS (Table-2).

Prognostic significance of hemoglobin-to-RDW ratio for OS

The median OS for the entire cohort was 10.0 months (95% CI, 4.3–15.7). Patients with a high hemoglobin-to-RDW ratio (HRR ≥ 0.7) had significantly longer OS compared with those with a low HRR (< 0.7) (median, 18.7 months [95% CI,

8.8–28.6] vs. 6.0 months [95% CI, 4.4–7.6]; p < 0.001; Figure-2).

In the univariate analysis, poor ECOG performance status (≥2; HR = 3.47, 95% CI 2.09–5.75; p < 0.001), presence of ≥3 metastatic sites (HR = 2.55, 95% CI 1.56–4.18; p = 0.001), low hemoglobin (HR = 1.99, 95% CI 1.17–3.41; p = 0.011), high RDW (HR = 1.77, 95% CI 1.04–3.01; p = 0.036), low HRR (HR = 2.70, 95% CI 1.71–4.26; p = 0.001), and elevated NLR (HR = 1.84, 95% CI 1.15–2.94; p = 0.011) were significantly associated with shorter OS.

To address potential covariance between hemoglobin and RDW, two separate multivariate models were constructed. In Model 1 (including Hb and RDW), ECOG performance status ≥2 (HR = 3.05, 95% CI 1.79–5.20; p < 0.001) and ≥3 metastatic sites (HR = 2.08, 95% CI 1.25–3.48; p = 0.005) remained independent predictors of inferior OS. In Model 2 (including HRR instead of Hb and RDW), ECOG performance status ≥2 (HR = 3.06, 95% CI 1.82–5.16; p < 0.001), ≥3 metastatic sites (HR = 1.95, 95% CI 1.17–3.29; p = 0.011), and low HRR (HR = 2.87, 95% CI 1.79–4.58; p < 0.001) were identified as independent prognostic factors for shorter OS (Table-4).

Table-1. Patient demographics and baseline clinical characteristics

Variable	n (%) / Median (IQR)
Age, years	
Median (IQR)	64.8 (59.8–69.9)
<65	58 (50.9)
≥65	56 (49.1)
Gender	
Male	91 (79.8)
Female	23 (20.2)
ECOG performance status	
0–1	88 (77.2)
≥2	26 (22.8)
Histologic subtype	
Adenocarcinoma	55 (48.2)
Squamous cell carcinoma	32 (28.1)
Unknown	27 (23.7)
PD-L1 expression	
Negative	37 (32.5)
1–49%	16 (14.0)
≥50%	28 (24.6)
Unknown	33 (28.9)
Brain metastasis	
Present	24 (21.1)
Absent	90 (78.9)
Number of metastatic sites	
<3	48 (42.1)
≥3	66 (57.9)
Laboratory findings (at nivolumab start)	
Hemoglobin (g/dL), median (IQR)	11.2 (9.2–12.6)
RDW (%), median (IQR)	15.4 (14.1–17.7)
Hb/RDW ratio, median (IQR)	0.74 (0.57–0.85)
≥0.7	48 (42.1)
<0.7	66 (57.9)
NLR, median (IQR)	3.8 (1.9–5.6)
>5	36 (31.6)
≤5	78 (68.4)
Progression	
Absent	17 (14.9)
Present	97 (85.1)
Vital status	
Alive	36 (31.6)
Deceased	78 (68.4)

Abbreviations: IQR, interquartile range; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death-ligand 1; NLR, neutrophil-to-lymphocyte ratio; RDW, red cell distribution width; HRR, hemoglobin-to-RDW ratio.

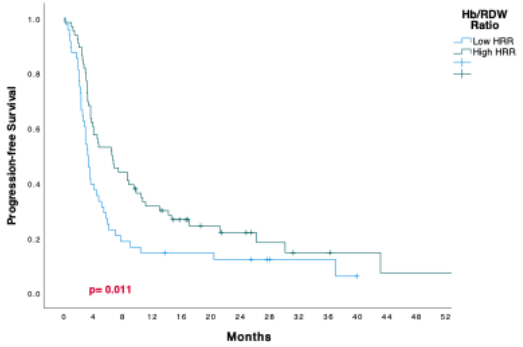

Figure-1. Progression-free survival by HRR group.

Table-2. Univariate and multivariate Cox regression analyses of factors associated with PFS in patients treated with second-line nivolumab.

Variable	Comparison	Univariate HR (95% CI)	p value	Multivariate HR (95% CI)	p value
Age group	≥65 vs <65	1.03 (0.69–1.54)	0.879		
Gender	Male vs Female	1.29 (0.80–2.08)	0.303		
ECOG performance status	≥2 vs 0–1	2.94 (1.83–4.71)	**<0.001**	2.71 (1.48-4.96)	**0.010**
Histologic subtype	Squamous vs Adenocarcinoma	1.27 (0.73–2.23)	0.395		
	Unknown vs Adenocarcinoma	0.92 (0.54–1.55)	0.743		
PD-L1 expression					
	1–49% vs Negative	0.60 (0.30–1.18)	0.139		
	≥50% vs Negative	0.70 (0.41–1.22)	0.207		
PD-L1 (binary)	Negative vs Positive	1.51 (0.93–2.45)	0.096	1.28 (0.78-2.10)	0.324
Brain metastasis	Present vs Absent	0.96 (0.59–1.58)	0.889		
Number of metastatic sites	≥3 vs <3	1.76 (1.16–2.67)	**0.007**	1.73 (1.01-2.98)	**0.047**
Hemoglobin	Low vs Normal	0.72 (0.46–1.12)	0.150		
RDW	High vs Low	1.36 (0.87–2.15)	0.177		
Hb/RDW ratio (HRR)	<0.7 vs ≥0.7	1.68 (1.21–2.53)	**0.012**	2.00 (1.21-3.30)	**0.007**
NLR	≥5 vs <5	1.13 (0.73-1.74)	0.591		

Abbreviations: HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed death-ligand 1; RDW, red cell distribution width; HRR, hemoglobin-to-RDW ratio. **Bold values indicate statistically significant results (p < 0.05).**

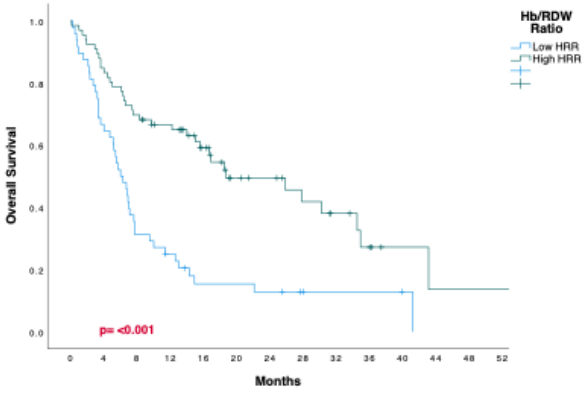

Figure-2. Overall survival by HRR group.

DISCUSSION

In this retrospective analysis of patients with advanced NSCLC treated with second-line nivolumab, we found that a higher baseline hemoglobin-to–red cell distribution width ratio was significantly associated with prolonged progression-free and overall survival. These findings suggest that HRR, a straightforward hematologic metric that combines hemoglobin and red cell distribution width, could be a useful prognostic indicator in the context of immunotherapy.

Our results are consistent with earlier studies demonstrating HRR's predictive value for various cancer types. Low HRR is independently associated with poorer progression-free and overall survival in patients undergoing systemic therapy, including immunotherapy, according to several studies on thoracic malignancies (14). Previous investigations shown HRR to be a significant predictor of survival outcomes in advanced non-small cell lung cancer (NSCLC), and similar findings were found in small-cell lung cancer cohorts (17, 18). Furthermore, Petrella et al. found that patients with low preoperative HRR had a recurrence risk that was more than double that of patients with higher ratios in surgically resected early-stage NSCLC (19). When taken as a whole, these findings support HRR as a repeatable and widely used prognostic indicator for lung cancer.

HRR's predictive importance probably comes from the way it reflects the patient's nutritional state and level of inflammation. In cancer patients with systemic inflammation or advanced disease, anemia and anisocytosis (high RDW) are frequently seen (14). Chronic inflammation can suppress erythropoiesis and cause functional iron deficiency, leading to anemia of chronic disease, while also releasing cytokines that disrupt erythrocyte maturation, elevating RDW (20). Thus, a low HRR may serve as a surrogate for an underlying proinflammatory and malnourished state. The effectiveness of immunotherapy and immune competence may be hampered by this environment; in fact, it is well recognized that poor outcomes in a variety of malignancies are correlated with elevated inflammatory indices, such as neutrophil counts, C-reactive protein, and LDH (21-23). On the other hand, people with higher HRR probably have superior bone marrow function and less systemic inflammation, which may result in more potent immune responses against tumors (24). Furthermore, patients with higher hemoglobin levels (high HRR) may have a tumor microenvironment more favorable to the effectiveness of immunotherapy since severe anemia might encourage tumor hypoxia and immune suppression (14). In summary, the HRR encapsulates valuable information about tumor–host dynamics: it integrates aspects of inflammation, nutritional status, and overall physiological reserve, all of which are critical determinants of prognosis in cancer therapy.

Several other peripheral blood markers have been explored as prognostic indicators in immunotherapy-treated NSCLC. For example, a high neutrophil-to-lymphocyte ratio (NLR) has been repeatedly associated with worse survival outcomes. In one cohort of nivolumab-treated NSCLC patients, those with a baseline NLR ≥5 had significantly shorter median overall survival (5.5 vs 8.4 months) and progression-free survival compared to patients with NLR <5 (25). Composite indices like the Lung Immune Prognostic Index (LIPI), which combines derived NLR and lactate dehydrogenase (LDH) levels, likewise stratify patients' outcomes on immunotherapy (13). A "poor" LIPI (dNLR >3 plus high LDH) correlates with a lower disease control rate and shorter survival on PD-1/PD-L1 inhibitors. In our study, although elevated NLR and low HRR were both associated with worse survival in univariate analyses, only HRR remained an independent prognostic factor for both PFS and OS in multivariate models. In contrast, NLR did not retain statistical significance in the multivariate analysis. These findings suggest that HRR may offer additional or superior prognostic value compared to traditional inflammation-based markers. Unlike NLR or LIPI, which predominantly reflect systemic inflammation, HRR also captures elements of anemia and red cell distribution variability, potentially providing a more integrated view of patient status.

This study has several limitations that should be acknowledged. As a single-center, retrospective analysis, it is inherently subject to selection bias, institutional practice patterns, and unmeasured confounders, which may limit the internal validity and generalizability of the findings. The relatively small number of female patients further restricts extrapolation across sexes and highlights the need for more balanced cohorts in future research. Additionally, while we applied a previously reported HRR cutoff, no standardized

threshold currently exists for this marker in NSCLC, and its optimal stratification value may vary depending on clinical context. Prospective studies are needed to refine and validate such thresholds. Finally, although HRR is easily derived from routine blood counts, it may be affected by chronic comorbidities or latent micronutrient deficiencies (e.g., iron, folate, B12), which were not systematically assessed and could introduce residual confounding.

CONCLUSION

In conclusion, baseline HRR appears to be a simple, inexpensive, and independent prognostic marker in advanced NSCLC patients treated with second-line nivolumab, warranting further prospective validation in larger, multi-center cohorts.

Conflict of Interest: The authors declare that they have no conflicts of interest.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2024;74(3):229-63.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2021;71(3):209-49.
3. Schabath MB, Cote ML. Cancer progress and priorities: lung cancer. Cancer epidemiology, biomarkers & prevention. 2019;28(10):1563-79.
4. Brahmer J, Reckamp KL, Baas P, Crinò L, Eberhardt WE, Poddubskaya E, et al. Nivolumab versus docetaxel in advanced squamous-cell non–small-cell lung cancer. New England Journal of Medicine. 2015;373(2):123-35.
5. Borghaei H, Paz-Ares L, Horn L, Spigel DR, Steins M, Ready NE, et al. Nivolumab versus docetaxel in advanced nonsquamous non–small-cell lung cancer. New England Journal of Medicine. 2015;373(17):1627-39.
6. Herbst RS, Baas P, Kim D-W, Felip E, Pérez-Gracia JL, Han J-Y, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. The lancet. 2016;387(10027):1540-50.
7. Rittmeyer A, Barlesi F, Waterkamp D, Park K, Ciardiello F, Von Pawel J, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. The Lancet. 2017;389(10066):255-65.
8. Wang H, Niu X, Jin Z, Zhang S, Fan R, Xiao H, Hu SS. Immunotherapy resistance in non-small cell lung cancer: from mechanisms to therapeutic opportunities. Journal of Experimental & Clinical Cancer Research. 2025;44(1):250.
9. Yang X, Luo B, Tian J, Wang Y, Lu X, Ni J, et al. Biomarkers and ImmuneScores in lung cancer: predictive insights for immunotherapy and combination treatment strategies. Biological Procedures Online. 2025;27(1):1-18.
10. Wojas-Krawczyk K, Kubiatowski T. Imperfect predictors for lung cancer immunotherapy—A field for further research. Frontiers in oncology. 2020;10:568174.
11. Topalian SL, Taube JM, Anders RA, Pardoll DM. Mechanism-driven biomarkers to guide immune checkpoint blockade in cancer therapy. Nature Reviews Cancer. 2016;16(5):275-87.
12. Longueville E, Dewolf M, Dalstein V, Durlach A, Vivien A, Nawrocki-Raby B, et al. Comparing neutrophil-to-lymphocyte ratio (NLR), absolute neutrophil count (ANC) and derived NLR as predictive biomarkers in first-line immunotherapy for non-small cell lung cancer: a retrospective study. Translational Lung Cancer Research. 2025;14(4):1212.
13. Mezquita L, Auclin E, Ferrara R, Charrier M, Remon J, Planchard D, et al. Association of the lung immune prognostic index with immune checkpoint inhibitor outcomes in patients with advanced non–small cell lung cancer. JAMA oncology. 2018;4(3):351-7.
14. Coradduzza D, Medici S, Chessa C, Zinellu A, Madonia M, Angius A, et al. Assessing the predictive power of the hemoglobin/red cell distribution width ratio in cancer: a systematic review and future directions. Medicina. 2023;59(12):2124.

15. Chi G, Lee JJ, Montazerin SM, Marszalek J. Prognostic value of hemoglobin-to-red cell distribution width ratio in cancer: a systematic review and meta-analysis. Biomarkers in Medicine. 2022;16(6):473-82.
16. Giudice GC, Rebuzzi SE, Mazzaschi G, Pecci F, Maffezzoli M, Acunzo A, et al. The prognostic value of the Haemoglobin/Red cell Distribution Width Ratio in a cohort of pre-treated patients with Renal Cell Carcinoma receiving nivolumab. Cancer Treatment and Research Communications. 2025:100927.
17. Pecci F, Mazzaschi G, Dodi A, Tamarozzi P, Manini M, Peroni M, et al. EP. 11.05 Prognostic Value of Hb/RDW and Its Correlation With Immune-Inflammatory Profile in NSCLC Receiving First-Line Immunotherapy. Journal of Thoracic Oncology. 2025;20(10):S784.
18. Wu F, Yang S, Tang X, Liu W, Chen H, Gao H. Prognostic value of baseline hemoglobin-to-red blood cell distribution width ratio in small cell lung cancer: A retrospective analysis. Thoracic Cancer. 2020;11(4):888-97.
19. Petrella F, Casiraghi M, Radice D, Cara A, Maffeis G, Prisciandaro E, et al. Prognostic value of the hemoglobin/red cell distribution width ratio in resected lung adenocarcinoma. Cancers. 2021;13(4):710.
20. Koma Y, Onishi A, Matsuoka H, Oda N, Yokota N, Matsumoto Y, et al. Increased red blood cell distribution width associates with cancer stage and prognosis in patients with lung cancer. PloS one. 2013;8(11):e80240.
21. McMillan DC. The systemic inflammation-based Glasgow Prognostic Score: a decade of experience in patients with cancer. Cancer treatment reviews. 2013;39(5):534-40.
22. Petrelli F, Cabiddu M, Coinu A, Borgonovo K, Ghilardi M, Lonati V, Barni S. Prognostic role of lactate dehydrogenase in solid tumors: a systematic review and meta-analysis of 76 studies. Acta oncologica. 2015;54(7):961-70.
23. Şahin G, Acar C, Yüksel HÇ, Tunbekici S, Açar FP, Çelebi G, Karaca B. Dynamic blood-based biomarkers predict early response to ipilimumab and nivolumab in advanced melanoma. Clinical and Translational Oncology. 2025:1-10.
24. Sun P, Zhang F, Chen C, Bi X, Yang H, An X, et al. The ratio of hemoglobin to red cell distribution width as a novel prognostic parameter in esophageal squamous cell carcinoma: a retrospective study from southern China. Oncotarget. 2016;7(27):42650.
25. Bagley SJ, Kothari S, Aggarwal C, Bauml JM, Alley EW, Evans TL, et al. Pretreatment neutrophil-to-lymphocyte ratio as a marker of outcomes in nivolumab-treated patients with advanced non-small-cell lung cancer. Lung cancer. 2017;106:1-7.