

# Pretreatment Fibrinogen-Albumin Ratio (FAR) Associated with Treatment Response and Survival in Advanced Non-Small Cell Lung Cancer Patients Treated with First-Line Anti-PD-1 Therapy Plus Platinum-Based Combination Chemotherapy

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**Purpose:** PD-1 inhibitors have been routinely used to treat advanced non-small cell lung cancer (NSCLC) and have significantly improved clinical outcomes. In this study, we aimed to explore the influence of pretreatment fibrinogen-albumin ratio (FAR) on treatment response and survival in advanced NSCLC patients treated with first-line anti-PD-1 therapy plus platinum-based combination chemotherapy.

**Patients and Methods:** A total of 91 patients with advanced NSCLC were included in the study. All patients received at least two cycles of systemic first-line anti-PD-1 therapy plus platinum-based combination chemotherapy. Receiver operating characteristics analysis was performed to determine the optimal cutoff values of FAR. Univariate and multivariate analyses were used to identify independent prognostic factors, and the Kaplan–Meier method was used to estimate survival curves.

**Results:** Multivariate logistic regression analysis showed that N stage (N2-3) and high FAR ( $\geq 0.175$ , optimal cutoff value) were independent predictors for objective response rate ( $P = 0.0002$ ,  $P = 0.0005$ , respectively). Multivariate Cox regression analysis of progression-free survival and overall survival showed that high FAR ( $\geq 0.145$ ) was independent prognostic factors ( $P = 0.0061$ ,  $P = 0.0024$ , respectively). Progression-free survival and overall survival were significantly shorter in the high FAR ( $\geq 0.145$ ) group than those in the low FAR ( $< 0.145$ ) group ( $P = 0.0024$ ,  $P = 0.0024$ , respectively).

**Conclusion:** Pretreatment FAR was an independent predictor for treatment response and independent prognostic factors in advanced NSCLC patients treated with first-line anti-PD-1 therapy plus platinum-based combination chemotherapy.

**Keywords:** non-small cell lung cancer, serum albumin, plasma fibrinogen, immunotherapy, prognosis

## Introduction

In patients with advanced non-small cell lung cancer (NSCLC) and PD-L1 TPS  $\geq 50\%$ , immune checkpoint inhibitors (ICIs) monotherapy was associated with significantly longer progression-free survival (PFS) and overall survival (OS) than those treated with platinum-based chemotherapy. However, ICIs alone may not be the best option for patients with PD-L1 TPS between 1% and 49%.<sup>1,2</sup> In addition, it was reported that ICIs combination chemotherapy has shown its significant benefits regardless of PD-L1 expression status, without inducing concomitant side effects and financial burden for the patients.<sup>3–7</sup> Therefore, identifying novel reliable, economic, and easily accessible biomarkers for advanced NSCLC patients treated with ICIs combination chemotherapy is essential.

Fibrinogen is an extracellular matrix protein composed of three polypeptide chains with fibrinogen alpha, beta, and gamma. Alpha may play a suppressive role in lung adenocarcinoma cells to inhibit tumor growth and metastasis through induction of apoptosis and inhibition of epithelial-mesenchymal transition.<sup>8</sup> Fibrinogen, as a molecule produced by the liver in response to cytokine stimulation, could also reflect the status of the tumor-associated inflammatory response.<sup>9</sup> Many tumor-growth and metastasis-enhancing events always occur during the tumor-associated inflammatory response, such as the inhibition of apoptosis, the enactment of immunosuppressive effects, the increased release of cytokines and inflammatory mediators.<sup>10</sup> Several studies have confirmed the relationship between high serum fibrinogen levels and poor outcomes in many kinds of solid malignancies, including NSCLC,<sup>11,12</sup> bladder cancer,<sup>13</sup> colorectal cancer,<sup>14</sup> and prostate cancer.<sup>15</sup>

Albumin plays a key role in the transport of chemotherapeutic drugs, binding to and being delivered by albumin can significantly affect their efficacy. Meanwhile, albumin can also bind to fatty acids, which can affect tumor proliferation and metabolism.<sup>16</sup> It was reported that albumin, which reflects nutritional status, was also closely related to the prognosis of many kinds of solid malignancies, including NSCLC,<sup>17–19</sup> Laryngeal Carcinoma,<sup>20</sup> prostate cancer,<sup>15</sup> upper tract urothelial Carcinoma,<sup>21</sup> gastric cancer.<sup>22</sup>

Several studies have confirmed the relationship between high fibrinogen-albumin ratio (FAR) and poor outcomes in many kinds of solid malignancies, including pancreatic neuroendocrine neoplasms,<sup>23</sup> gastrointestinal stromal tumors,<sup>24</sup> locally advanced rectal cancer,<sup>25</sup> Glioblastoma.<sup>26</sup> It was also reported that FAR was independently associated with PFS in EGFR-Mutant lung adenocarcinoma patients receiving first-line EGFR-TKIs treatment.<sup>27</sup> However, the prognostic values of FAR in advanced NSCLC patients treated with first-line anti-PD-1 therapy plus platinum-based combination chemotherapy is still unknown.

Thus, we conducted this retrospective study to mainly discuss correlations of pretreatment FAR with treatment response and survival in advanced NSCLC patients treated with first-line anti-PD-1 therapy plus platinum-based combination chemotherapy.

## Materials and Methods

### Patients and Samples

A total of 91 patients with advanced NSCLC who could not receive radical surgery or radiotherapy at baseline and received systemic anti-PD-1 therapy (camrelizumab, sintilimab, pembrolizumab, tislelizumab or toripalimab) plus platinum-based combination chemotherapy as the first-line setting at Guangxi Medical University Affiliated Tumor Hospital between April 2019 and July 2021 were enrolled. Patients received 200mg camrelizumab, 200mg sintilimab, 200mg pembrolizumab, 200mg tislelizumab or 240mg toripalimab intravenously once every 3 weeks. Combination chemotherapy was all based on platinum doublet chemotherapy. The other chemotherapy drugs, including pemetrexed, paclitaxel/nab-paclitaxel, docetaxel, and gemcitabine, were chosen by physicians according to clinical treatment guidelines. Patients with histories of other malignant tumors, chronic inflammatory diseases, current steroid therapy, acute infection, or deep vein thrombosis were excluded.

Clinicopathological characteristics of the patients, including age at the time of treatment, sex, smoking history, Eastern Cooperative Oncology Group score (ECOG score), histology, TNM stage, and radiotherapy were collected through electronic medical records. Plasma fibrinogen and serum albumin were collected before treatment and FAR was defined as fibrinogen-albumin ratio. Whole-body computed tomography scans were performed every 6–8 weeks after two cycles of treatment to assess patients' response to treatment according to The Response Evaluation Criteria in Solid Tumors (RECIST, version 1.1). The last follow-up date was July 1, 2021. Objective response rate (ORR) was defined as complete remission + partial remission. Progression-free survival (PFS) was defined as the time from initial treatment to imaging progression, death, or the last follow-up. Overall survival (OS) was defined as the time from initial treatment to the last follow-up or death, whichever came first.

This study was conducted following the principles of the Declaration of Helsinki and approved by the Ethics Committee of Guangxi Medical University Affiliated Tumor Hospital (Approval number: LW2021102). The identifiable information of patients was unnamed or anonymous to protect patients' privacy. The need for informed consent was waived owing to the retrospective nature of the study.

## Statistical Analysis

The baseline characteristics and treatment response of the patients were reported as medians and interquartile ranges for continuous variables, or frequencies and percentages for categorical variables. Receiver operating characteristics analysis was performed to determine the optimal cutoff values of FAR. Univariate and multivariate logistic regression were used to identify independent predictors between clinical factors/FAR (0.175, optimal cutoff value) and ORR. For the survival outcomes, we used the Kaplan–Meier method to generate the PFS and OS survival curves and the Log rank test to compare survival outcomes among patients separated by FAR (0.145, optimal cutoff value). Univariate and multivariate Cox proportional hazards regression analysis used the backward elimination method to estimate hazard ratios for risk factors. Variables included in the multivariable analysis were selected based on the influence of introducing covariates in the basic model or eliminating covariates in the complete model on the regression coefficient >10% and statistical significance in the univariable analysis ( $P < 0.10$ ).  $P < 0.05$  was considered statistically significant. All tests were two-sided. All data were analyzed using the statistical package R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria) and Empower (X&Y Solutions, Inc. Boston, Massachusetts).

## Results

### Patients' Clinicopathological Characteristics and Treatment Response

The clinicopathological characteristics and treatment response of the 91 advanced NSCLC patients are listed in Table 1. Twenty-three (25.27%) female patients and 68 (74.73%) male patients were included. The age of patients ranged from 32 to 80 years, and the median was 61 years. Fifty-nine (64.84%) patients had a history of smoking. Eighty-four (92.31%) patients had the ECOG score of 0–1. Forty (43.96%) patients had the histologic type of squamous cell carcinoma (SCC), while 48 (56.04%) patients were diagnosed with Non-SCC (53.8%). Twenty-two (24.18%) patients had the T stage of

**Table 1** Patients' Clinicopathological Characteristics and Treatment Response

Variables		Value or N (%)
Sex	Female	23(25.27)
	Male	68 (74.73)
Age(years)	Mean $\pm$ Standard Deviation	59.15 $\pm$ 9.74
	Median (range)	61.00 (32.00–80.00)
Smoking history	No	32 (35.16)
	Yes	59 (64.84)
ECOG score	0–1	84 (92.31)
	2–3	7 (7.69)
Histology	Non-SCC	48 (56.04)
	SCC	40 (43.96)
T stage	T1–2	22 (24.18%)
	T3–4	69 (75.82%)
N stage	N0–1	16 (17.58%)
	N2–3	75 (82.42%)
TNM stage	III	24 (26.37)
	IV	67 (73.63)
Radiotherapy	No	77 (84.62)
	Yes	14 (15.38)
FAR	Mean $\pm$ Standard Deviation	0.14 $\pm$ 0.05
	Median (range)	0.13 (0.04–0.35)
Best response	CR	0 (0)
	PR	50 (54.95)
	SD	36 (39.56)
	PD	5 (5.49)

**Abbreviations:** ECOG score, Eastern Tumor Cooperation Group score; SCC, squamous cell carcinoma; Non-SCC, none squamous cell carcinoma; TNM, tumor, node, and metastases; FAR, fibrinogen-albumin ratio; CR, complete remission; PR, partial remission; SD, stable disease; PD, disease progression.

T1-2, while 69 (75.82%) had the T stage of T3-4. 16 (17.58%) patients had the N stage of N0-1, while 75 (82.42%) had the N stage of T2-3. 24 (26.37%) patients had the TNM stage of III, while 67 (73.63%) had the TNM stage of IV. 14 (15.38%) patients had a history of radiotherapy. The FAR ranged from 0.04 to 0.35, and the median was 0.13. The treatment response, CR 0(0%), PR 50 (54.95%), SD 36 (39.56%), and PD 5 (5.49%).

## The Optimal Cutoff Values of FAR

The optimal cutoff value of FAR to predict ORR was 0.175 (AUC: 0.6407, sensitivity: 0.9000, specificity: 0.3659) ([Supplemental Figure 1](#)). The optimal cutoff values of FAR to predict PFS was 0.145 (AUC: 0.7170, sensitivity: 0.6154, specificity: 0.8077) ([Supplemental Figure 2](#)). The optimal cutoff value of FAR to predict OS was 0.145 (AUC: 0.7251, sensitivity: 0.7407, specificity: 0.7812) ([Supplemental Figure 3](#)).

## Univariate and Multivariate Logistic Regression Analysis for ORR

The results of the univariate and multivariate logistic regression analyses are shown in [Table 2](#). In the univariate logistic regression models, N stage (N2-3), TNM stage IV and high FAR ( $\geq 0.175$ , optimal cutoff value) were significant predictors

**Table 2** Univariate and Multivariate Analyses for ORR in Patients with NSCLC

Variables	N (%)	Univariate Analysis	Multivariate Analysis
		OR (95% CI) P value	OR (95% CI) P value
Sex			
Female	23 (25.27%)	1.0	
Male	68 (74.73%)	1.47 (0.57, 3.79) 0.4285	
Age(years)			
<60	40 (43.96%)	1.0	
$\geq 60$	51 (56.04%)	1.71 (0.74, 3.96) 0.2076	
Smoking history			
No	32 (35.16%)	1.0	
Yes	59 (64.84%)	1.65 (0.69, 3.93) 0.2561	
ECOG score			
0-1	84 (92.31%)	1.0	
2-3	7 (7.69%)	0.59 (0.12, 2.80) 0.5073	
Histology			
Non-SCC	51 (56.04%)	1.0	
SCC	40 (43.96%)	1.73 (0.75, 4.03) 0.2011	
T stage			
T1-2	22 (24.18%)	1.0	
T3-4	69 (75.82%)	0.80 (0.30, 2.12) 0.6539	
N stage			
N0-1	16 (17.58%)	1.0	17.45 (3.78, 80.54) 0.0002
N2-3	75 (82.42%)	7.27 (1.91, 27.77) 0.0037	
TNM stage			
III	24 (26.37%)	1.0	
IV	67 (73.63%)	0.30 (0.11, 0.86) 0.0253	0.40 (0.10, 1.67) 0.2091
Radiotherapy			
No	77 (84.62%)	1.0	
Yes	14 (15.38%)	0.40 (0.12, 1.29) 0.1240	
FAR			
<0.175	71 (78.02%)	1.0	
$\geq 0.175$	20 (21.98%)	0.19 (0.06, 0.59) 0.0040	0.10 (0.03, 0.36) 0.0005

**Abbreviations:** ORR, objective response rate; NSCLC, non-small cell lung cancer; ECOG score, Eastern Tumor Cooperation Group score; SCC, squamous cell carcinoma; Non-SCC, none squamous cell carcinoma; TNM, tumor, node, and metastases; FAR, fibrinogen-albumin ratio.

for ORR (odds ratio [95% CI]: 7.27 [1.91, 27.77],  $p = 0.0037$ ; 0.30 [0.11, 0.86],  $P = 0.0253$ ; 0.217 [0.077–0.573],  $p = 0.002$ ; respectively). In the multivariate logistic regression model, N stage (N2–3) and high FAR ( $\geq 0.175$ , optimal cutoff value) were independent predictors for ORR (17.45[3.78, 80.54],  $P = 0.0002$ ; 0.10 (0.03, 0.36),  $P = 0.0005$ , respectively).

## Survival Analysis

Kaplan–Meier curves of PFS and OS stratified by FAR ( $\geq 0.145$  or  $< 0.145$ , optimal cutoff value) are shown in Figures 1 and 2. PFS and OS were significantly shorter in the high-FAR group than those in the low-FAR group ( $p = 0.0024$ ,  $p = 0.0024$ , respectively).

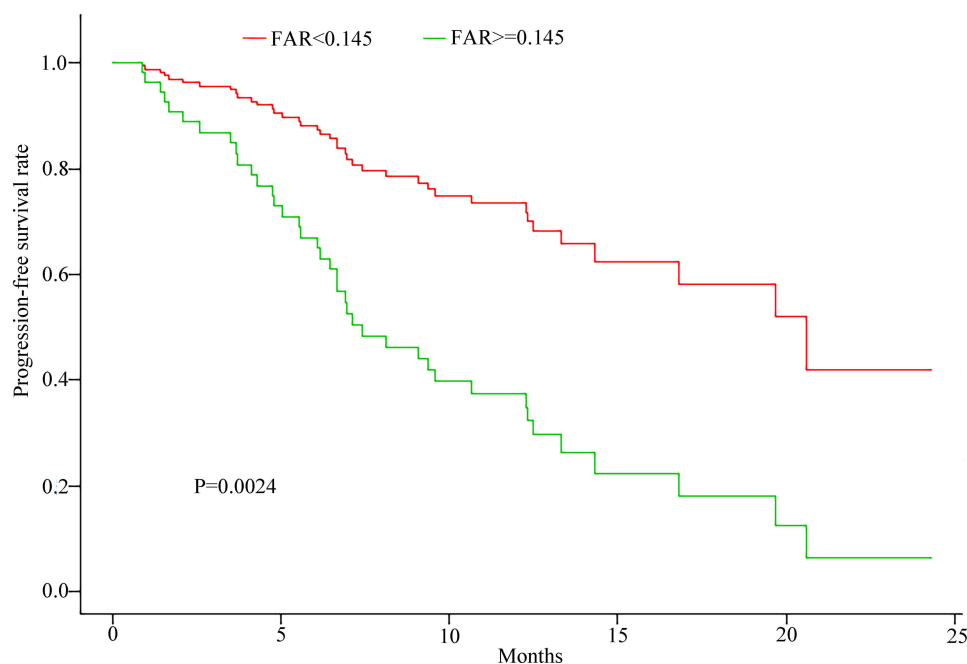
## Univariate and Multivariate Analyses for PFS and OS

In the univariate Cox proportional hazards regression analyses, high FAR ( $\geq 0.145$ , optimal cutoff value) was significant prognostic factors for PFS (hazard ratio (HR) [95% CI]: 2.60 [1.36, 4.98],  $P = 0.0038$ ). In the multivariate Cox proportional hazards regression analysis, high FAR ( $\geq 0.145$ , optimal cutoff value) was also independent prognostic factors for PFS (hazard ratio (HR) [95% CI]: 2.68 [1.33, 5.43],  $P = 0.0061$ ) (Table 3).

Univariate Cox proportional hazards regression analysis showed that radiotherapy and high FAR ( $\geq 0.145$ , optimal cutoff value) were significant prognostic factors for OS (2.55 [1.11, 5.86],  $P = 0.0268$ ; 3.74 [1.57, 8.90],  $P = 0.0028$ , respectively). Multivariate Cox proportional hazards regression analysis showed that high FAR ( $\geq 0.145$ , optimal cutoff value) also was significant prognostic factors for OS (4.95 [1.76, 13.89],  $P = 0.0024$ ) (Table 4).

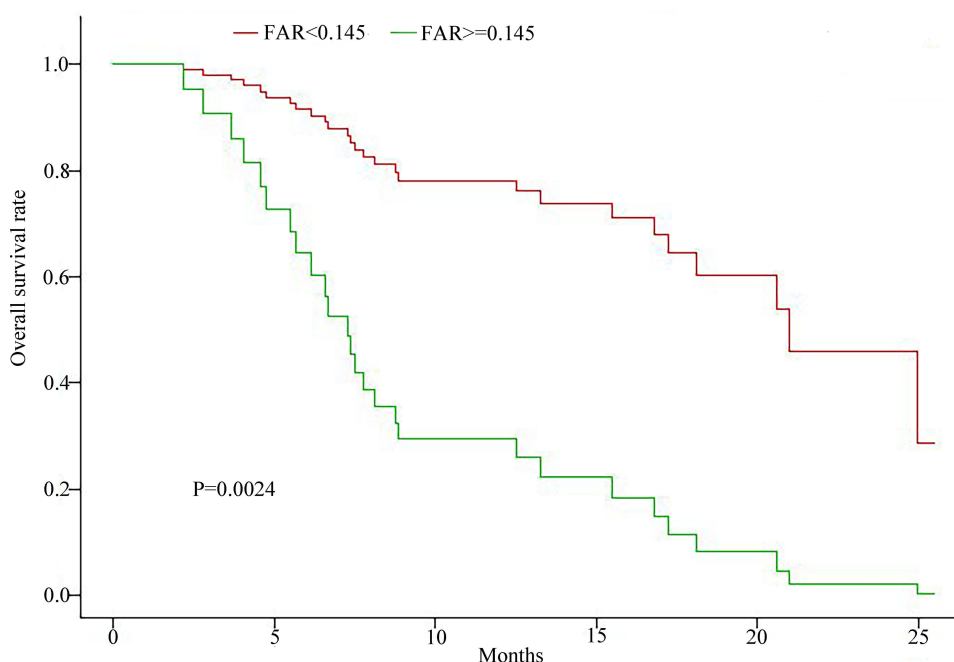
## Discussion

ICIs have become standard treatment options in patients with advanced NSCLC. It was reported that ICIs combination chemotherapy has shown significant benefits regardless of PD-L1 expression status.<sup>3–5,7,28</sup> However, only a minority of patients benefit from this novel and costly method of treatment. PD-L1 expression, tumor mutation burden, and lymphocytic tumor infiltration might be closely related to immunotherapy outcomes.<sup>28–31</sup> However, limited by cumbersome detection protocols and high costs, they are not considered to be perfect predictors. Therefore, easy, affordable, and efficient markers are needed to help characterize the patients who can potentially benefit from the ICIs treatment.



**Figure 1** Kaplan–Meier survival curves for PFS stratified by different values of FAR.

**Abbreviations:** PFS, progression-free survival; FAR, fibrinogen-albumin ratio.



**Figure 2** Kaplan-Meier survival curves for OS stratified by different values of FAR.

**Abbreviations:** OS, overall survival; FAR, fibrinogen-albumin ratio.

In recent years, it has been reported that peripheral blood biomarkers, including prognostic nutrition index, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and fibrinogen-to-lymphocyte ratio were suggestive indicators for the prognosis of advanced NSCLC patients treated with ICIs.<sup>32–34</sup> In our study, a total of 91 advanced NSCLC patients treated with first-line anti-PD-1 therapy plus platinum-based combination chemotherapy were included retrospectively. We found that high FAR ( $\geq 0.145$ ) was independent predictors for ORR and independent prognostic factors for PFS and OS. PFS and OS were significantly shorter in the high FAR group than those in the low FAR group. Lang et al found that decreasing leading serum tumor markers (STM) at first restaging predict longer PFS and OS among initial radiological non-responders in ICIs treated NSCLC patients.<sup>35</sup> Tang et al found that the combination score based on the dynamics of early STM and neutrophil-to-lymphocyte ratio can accurately predict the clinical efficacy of PD-1/PD-L1 inhibitors and prognosis in advanced NSCLC patients.<sup>36</sup> In our study, we found that FAR was independent predictors for ORR and independent prognostic factors for PFS and OS. The predictive role of STM dynamics, single or combination with FAR, further studies is needed in advanced NSCLC patients treated with first-line anti-PD-1 therapy plus platinum-based combination chemotherapy.

Fibrinogen, a molecule produced by the liver in response to cytokine stimulation, could reflect the status of the tumor-associated inflammatory response.<sup>9</sup> A high level of fibrinogen was associated with poor prognosis in NSCLC patients.<sup>11,12</sup> It was reported that nutrition as an important determinant of immune response and malnutrition was associated with impaired cell-mediated immunity against tumor progression and metastasis.<sup>37,38</sup> Low serum albumin, which reflects nutritional status, could predict poor prognosis in NSCLC patients.<sup>11,18</sup> As a composite indicator, FAR could represent the coagulation system, nutritional status, inflammation of a patient. Therefore, it is reasonable to adopt FAR as prognostic factors in advanced NSCLC patients treated with first-line anti-PD-1 therapy plus platinum-based combination chemotherapy.

In advanced NSCLC patients undergoing first-line platinum-based chemotherapy, Ying et al found that albumin-to-fibrinogen ratio (AFR) was independent risk factors for PFS and significant prognostic factors for OS. The PFS and OS in the high AFR group were significantly improved compared with those in the low AFR group.<sup>39</sup> In our study, all patients received systemic first-line anti-PD-1 therapy plus platinum-based combination chemotherapy. The FAR was independent risk factors for PFS and significant prognostic factors for OS. PFS and OS were significantly shorter in the

**Table 3** Univariate and Multivariate Analyses for PFS in Patients with NSCLC

Variables	N (%)	Univariate Analysis	Multivariate Analysis
		HR (95% CI) P value	HR (95% CI) P value
Sex			
Female	23 (25.27%)	1.0	
Male	68 (74.73%)	0.61 (0.31, 1.19) 0.1494	
Age(years)			
<60	40 (43.96%)	1.0	
≥60	51 (56.04%)	0.89 (0.47, 1.68) 0.7123	
Smoking history			
No	32 (35.16%)	1.0	
Yes	59 (64.84%)	0.86 (0.45, 1.64) 0.6511	
ECOG score			
0–I	84 (92.31%)	1.0	
2–3	7 (7.69%)	2.12 (0.88, 5.12) 0.0937	
Histology			
Non-SCC	51 (56.04%)	1.0	
SCC	40 (43.96%)	1.11 (0.59, 2.09) 0.7460	
T stage			
T1–2	22 (24.18%)	1.0	
T3–4	69 (75.82%)	2.10 (0.87, 5.03) 0.0971	
N stage			
N0–I	16 (17.58%)	1.0	
N2–3	75 (82.42%)	0.95 (0.42, 2.15) 0.8970	
TNM stage			
III	24 (26.37%)	1.0	
IV	67 (73.63%)	1.58 (0.72, 3.45) 0.2502	
Radiotherapy			
No	77 (84.62%)	1.0	
Yes	14 (15.38%)	2.03 (0.98, 4.22) 0.0565	
FAR			
<0.145	57 (62.64%)	1.0	
≥0.145	34 (37.36%)	2.60 (1.36, 4.98) 0.0038	2.68 (1.33, 5.43) 0.0061

**Abbreviations:** PFS, progression-free survival; NSCLC, non-small cell lung cancer; ECOG score, Eastern Tumor Cooperation Group score; SCC, squamous cell carcinoma; Non-SCC, none squamous cell carcinoma; TNM, tumor, node, and metastases; FAR, fibrinogen-albumin ratio.

high FAR ( $\geq 0.145$ ) group than those in the low FAR ( $< 0.145$ ) group, which was consistent with Ying et al. For patients undergoing first-generation EGFR-TKI (gefitinib, erlotinib, or icotinib) as the first-line treatment, Zhao et al found that FAR was independent prognostic factors for PFS, but not independently correlated with OS.<sup>27</sup> In our study, the FAR was independent prognostic factors for PFS, consistent with Zhao et al. Our study also found that FAR was independently correlated with OS. In addition, our study also found that high FAR was independent predictors for ORR. To the best of our knowledge, this study has firstly investigated the relationship between FAR and clinical outcomes in advanced NSCLC patients treated with anti-PD-1 therapy combination chemotherapy regimens. Our study demonstrated that FAR was independent predictors for treatment response and independent prognostic factors for PFS and OS in advanced NSCLC patients treated with anti-PD-1 therapy plus platinum-based combination chemotherapy. Therefore, FAR is expected to become a new biomarker for prognosis evaluation and treatment response prediction for advanced NSCLC patients and is significant in the guidance they could provide for the development of individualized treatment strategies.

Our study still has several limitations. First, this study was a single-center retrospective analysis and included a small number of patients. Therefore, multicentric prospective studies with large samples need to be carried out in the future.



**Table 4** Univariate and Multivariate Analyses for OS in Patients with NSCLC

Variables	N (%)	Univariate Analysis	Multivariate Analysis
		HR (95% CI) P value	HR (95% CI) P value
Sex			
Female	23 (25.27%)	1.0	
Male	68 (74.73%)	1.12 (0.45, 2.81) 0.8056	
Age (years)			
<60	40 (43.96%)	1.0	
≥60	51 (56.04%)	0.84 (0.39, 1.81) 0.6506	
Smoking history			
No	32 (35.16%)	1.0	
Yes	59 (64.84%)	1.01 (0.43, 2.33) 0.9901	
ECOG score			
0-1	84 (92.31%)	1.0	
2-3	7 (7.69%)	2.37 (0.94, 5.99) 0.0687	
T stage			
1-2	22 (24.18%)	1.0	
3-4	69 (75.82%)	1.04 (0.42, 2.62) 0.9275	
N stage			
0-1	16 (17.58%)	1.0	
2-3	75 (82.42%)	0.96 (0.36, 2.57) 0.9316	
TNM stage			
III	24 (26.37%)	1.0	
IV	67 (73.63%)	1.25 (0.50, 3.12) 0.6352	
Histology			
Non-SCC	51 (56.04%)	1.0	
SCC	40 (43.96%)	0.65 (0.30, 1.42) 0.2826	
Radiotherapy			
No	77 (84.62%)	1.0	
Yes	14 (15.38%)	2.55 (1.11, 5.86) 0.0268	2.21 (0.83, 5.86) 0.1110
FAR			
<0.145	57 (62.64%)	1.0	
≥0.145	34 (37.36%)	3.74 (1.57, 8.90) 0.0028	4.95 (1.76, 13.89) 0.0024

**Abbreviations:** OS, overall survival; NSCLC, non-small cell lung cancer; ECOG score, Eastern Tumor Cooperation Group score; SCC, squamous cell carcinoma; Non-SCC, none squamous cell carcinoma; TNM, tumor, node, and metastases; FAR, fibrinogen-albumin ratio.

Second, due to the lack of external data, we could not design a validation group to verify our findings. Third, due to the lack of external data, PD-L1 expression of tumors was not included in our study. All these may result in underestimating the association of PD-L1 expression with the antitumor effect using ICI treatment.

## Conclusion

Pretreatment FAR was an independent predictor for treatment response and independent prognostic factors in advanced NSCLC patients treated with first-line anti-PD-1 therapy plus platinum-based combination chemotherapy.

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## Disclosure

The authors report no conflicts of interest in this work.

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