

INTRODUCTION

China has been a major tobacco-consuming country and smoking remains the top risk factor for lung cancer.

We aimed to assess the impact of smoking status on survival in Chinese lung cancer patients.

METHODS

A total of **4325** lung cancer patients with determined smoking status were retrospectively identified at Zhongshan Hospital of Fudan University, Shanghai. Baseline covariates, including age, gender, cancer stage, cigarette smoking status (never, former, and current smoking status), cumulative cigarette smoking PYs, histology, PD-L1 expression, treatment strategies were documented. Based on cumulative PYs, patients were categorized as having never smoked or having a light (>0–20PYs), moderate (≥20–40PYs), or heavy (≥40PYs) cigarette smoking history. For patients who were former smokers, quit smoking time was specified and classified as ≤1 year, 1-5 years and ≥5 years. Overall survival (OS) and progression-free survival (PFS) were estimated by Kaplan-Meier curves.

DISCUSSION AND CONCLUSION

Take Away Message

- Smoking status impacts OS in stage III-IV lung cancer patients, whereas no significant association was observed in stage I-II patients.
- Short term smoking cessation (<1 year) correlates with the worst OS; longer quitting duration is linked to improved survival.
- For advanced stage patients on first line immunotherapy, smokers gain PFS benefit, but this does not translate into OS advantage.
- The combination of PD-L1 expression and smoking status has substantial predictive value for PFS among patients treated with immunotherapy.
- Smoking cessation remains an essential component of lung cancer management.

Future Directions

- Validate the prognostic value of combining PD-L1 and smoking status in larger real-world Chinese cohorts.
- Uncover underlying mechanisms of discordant PFS-OS among immunotherapy-treated smokers.
- Assess whether proactive smoking-cessation interventions improve long-term survival for immunotherapy-treated lung cancer patients.

REFERENCES & ACKNOWLEDGEMENTS

- [1] Fares AF, Li Y, Jiang M, Bet al. Association between duration of smoking abstinence before non-small-cell lung cancer diagnosis and survival: a retrospective, pooled analysis of cohort studies. *Lancet Public Health*. 2023 Sep;8(9):e691-e700.
- [2] Murray RL, O'Dowd E. Smoking cessation and lung cancer: never too late to quit. *Lancet Public Health*. 2023 Sep;8(9):e664-e665.
- [3] Hopkins AM, Abuhelwa AY, McKinnon RA, et al. Smoking and immunotherapy efficacy in lung cancer by PDL1 subgroups: An individual participant data meta-analysis of atezolizumab clinical trials: Smoking and immunotherapy efficacy in lung cancer. *Eur J Cancer*. 2022 Jan;160:279-281.

Artificial Intelligence (AI) Use Disclaimer

The authors declare that no AI tools have been employed in any stage of this work. All intellectual contributions, text, figures and conclusions are original from authors.

RESULTS

Table 1. Baseline Characteristics

	all patients (n=4325)	smokers (n=2522)	no-smokers (n=1803)	P value
Age (year)				
Median	65	65	65	
Range	17-98	28-88	17-98	
Gender				
Female	1406	50	1356	
Male	2919	2472	447	<0.0001
COPD				
yes	1046	811	235	
no	1723	889	834	<0.0001
unknown	1556			
Asthma				
yes	126	80	46	
no	4076	2354	1722	0.1987
unknown	123			
Emphysema				
yes	264	237	27	
no	3567	1873	1694	<0.0001
unknown	494			
Pathology				
Adenocarcinoma	2600	1081	1519	<0.0001
Squamous cell carcinoma	947	843	104	<0.0001
Adeno-squamous carcinoma	43	24	19	0.7384
Neuroendocrine carcinoma*	23	14	9	0.803
Sarcomatoid carcinoma	19	16	3	0.0329
NSCLC-NOS	56	46	10	0.0002
Small cell lung cancer	472	390	82	<0.0001
Large Cell Lung Carcinoma	63	52	11	<0.0001
undifferentiated carcinoma	24	23	1	<0.0001
others	78	33	45	
PD-L1 expression				
<1	1007	550	457	
1-49	737	447	290	
>49	386	269	117	<0.0001
unknown	2195			

* Indicates other subtypes of neuroendocrine carcinoma, excluding SCLC and LCLC

- Association between smoking status and OS in lung cancer patients:** The smoking status was not associated with the OS outcome in patients with Stage I and Stage II except for the patients with StagelII and Stage IV (**Fig.2**).

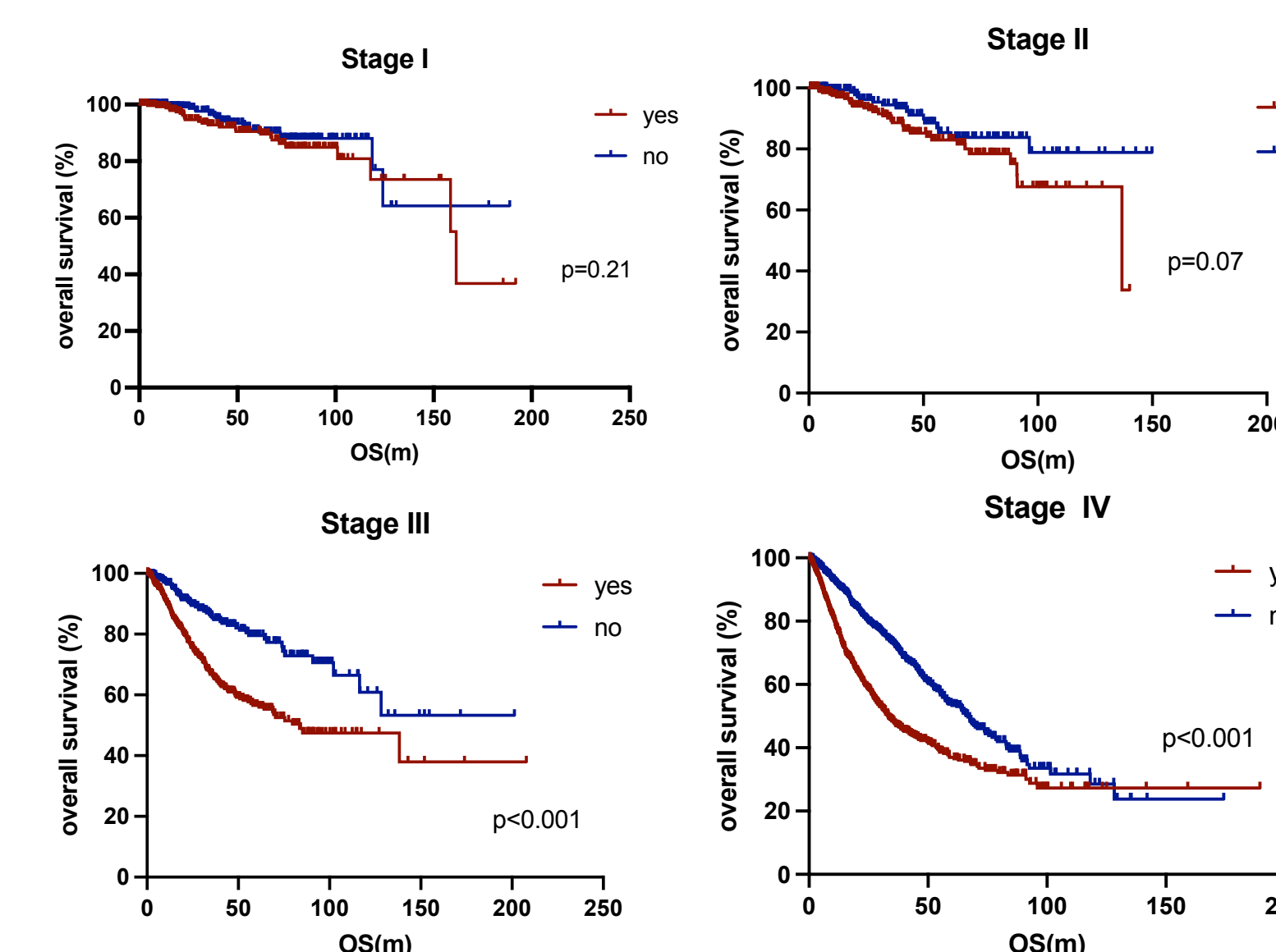


Figure 2. Association between smoking status and overall survival across different disease stages.

- Those who were current smokers had inferior OS outcome compared with those former and never-smokers (**Fig.3A**). Specifically, patients who quit smoking less than 1 year had shortest OS compared with those quit 1-5years and more than 5 years (**Fig.3B**)

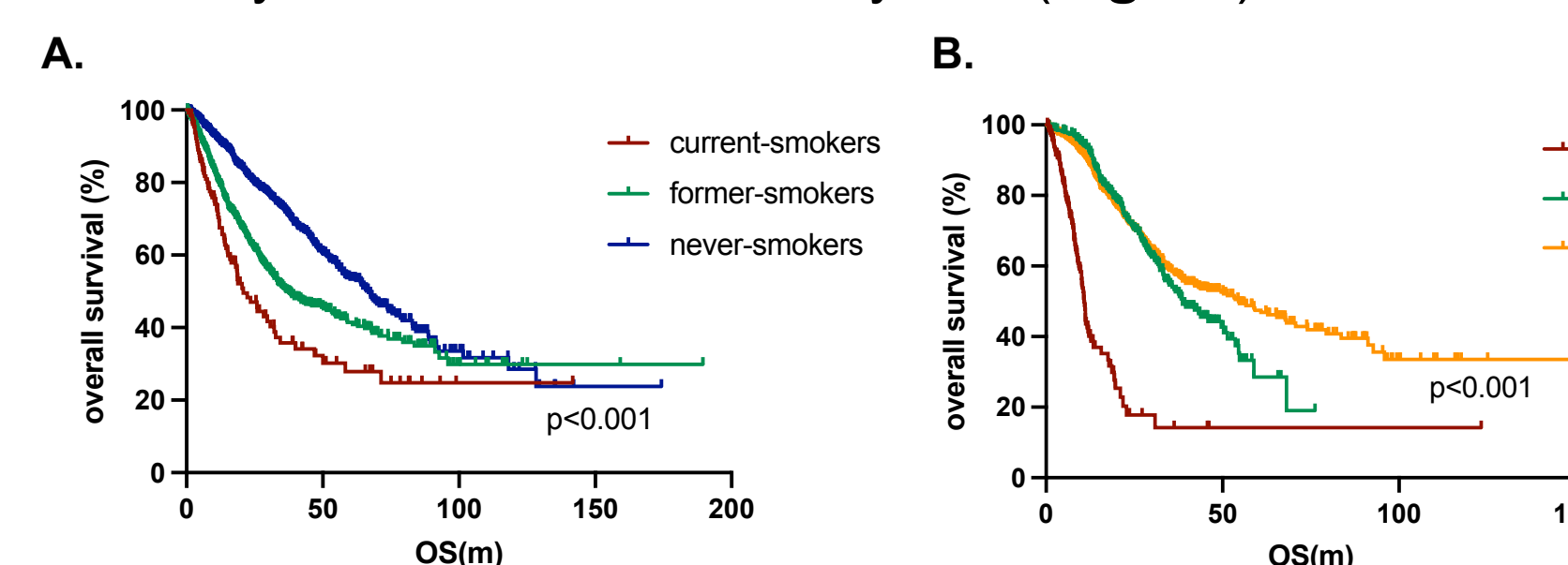


Figure 3. Survival outcomes according to smoking-cessation status and duration of smoking cessation.

Among 4325 lung cancer patients in our center:

- With the exception of patients with lung adenocarcinoma, among whom 58.4% were never-smokers, cases of lung squamous cell carcinoma, small cell lung cancer, pulmonary sarcomatoid carcinoma, large cell carcinoma ,NSCLC-NOS and undifferentiated carcinoma were predominantly current or former smokers.
- Smoking status was associated with PD-L1 expression, and smokers tended to have higher PD-L1 expression compared with non-smokers (p<0.01).

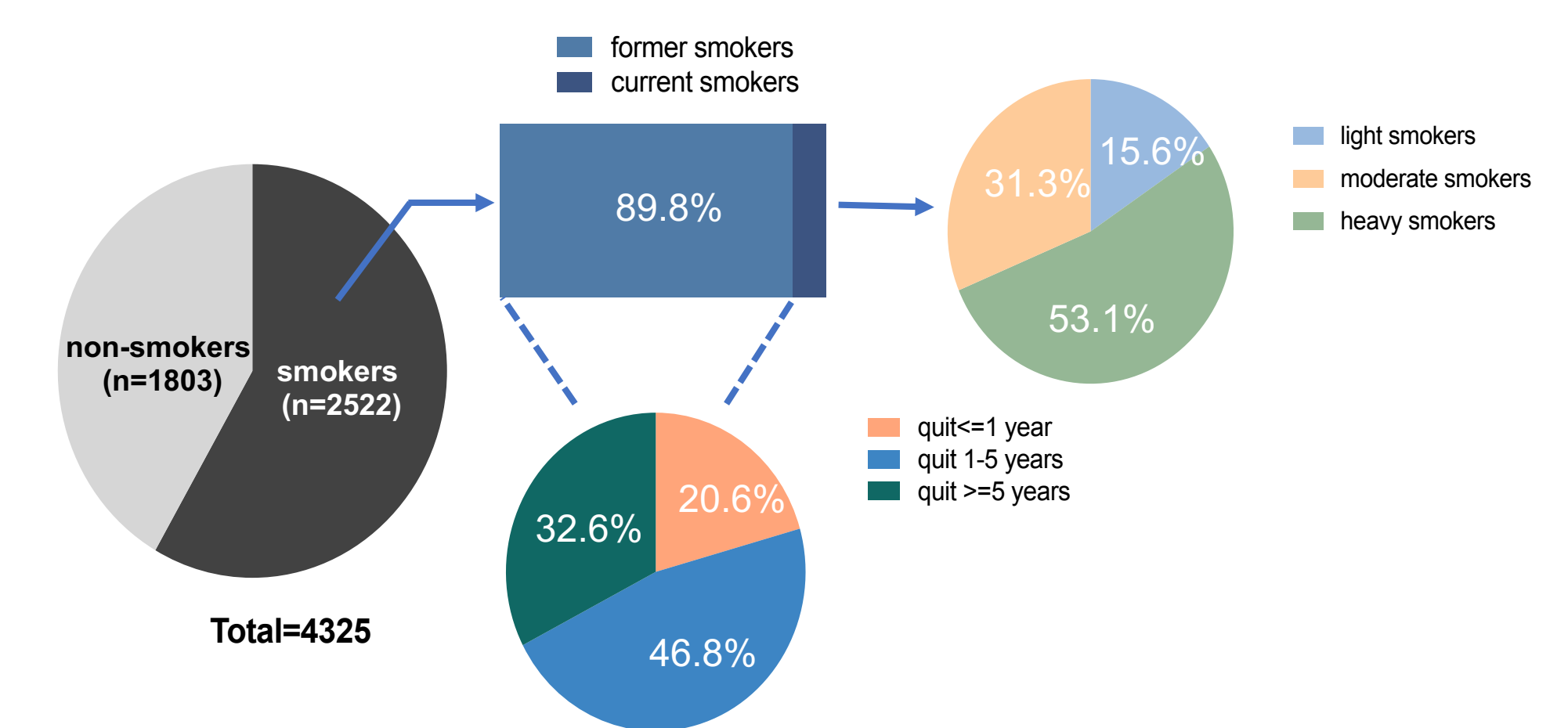


Figure 1. Distribution of patients with confirmed smoking history according to smoking status, smoking burden (pack-years), and duration of smoking cessation.

- In advanced lung cancer patients who were treated with first-line immunotherapy, smokers **had significantly PFS benefit** compared with non-smokers (**Fig.4A**), however, this initial response could not convert to long-term OS benefit. Conversely, smokers had **inferior OS** compared with non-smokers (**Fig.4B**).

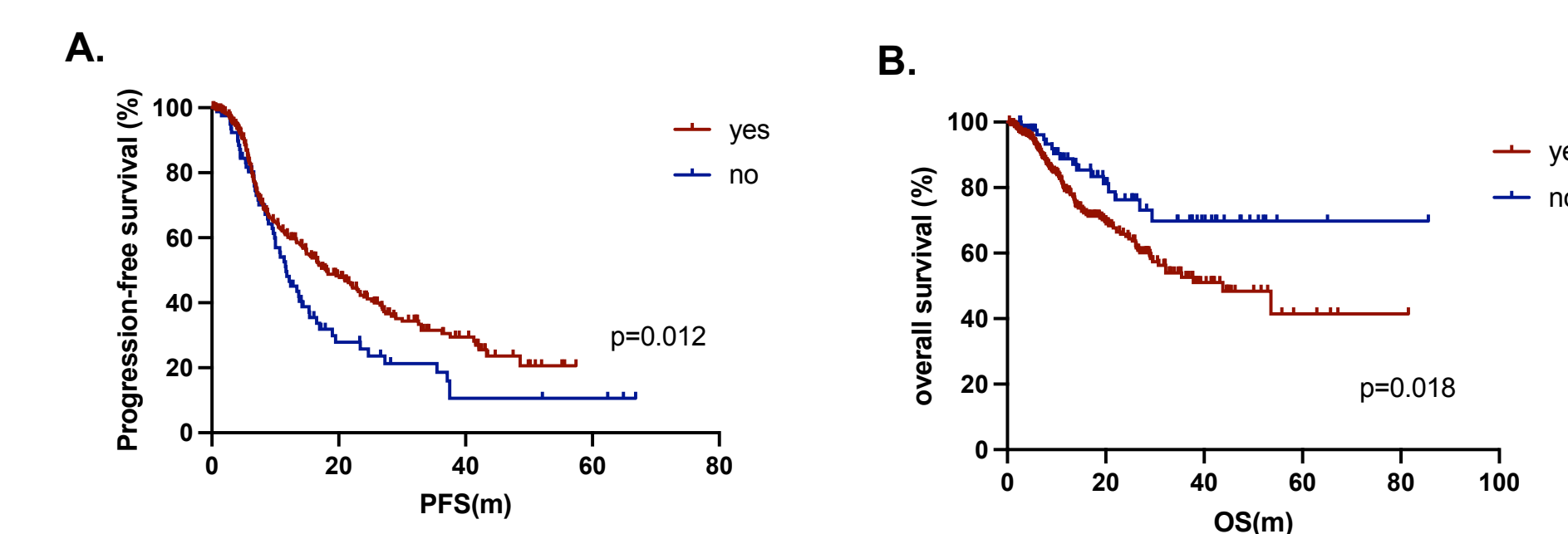


Figure 4. Impact of smoking status on PFS and OS in patients with lung cancer receiving immunotherapy.

- Impact of PD-L1+smoking status on survival outcome:** when we combined PD-L1 expression and smoking status into the prognosis model, we found smokers with ≥50% PD-L1 expression had longest PFS when treated with immunotherapy (**Fig.5A**). However, non-smokers with high PD-L1 expression could also benefit from immunotherapy in a long-term, whereas smokers with negative PD-L1 expression had inferior OS compared with other groups (**Fig.5B**).

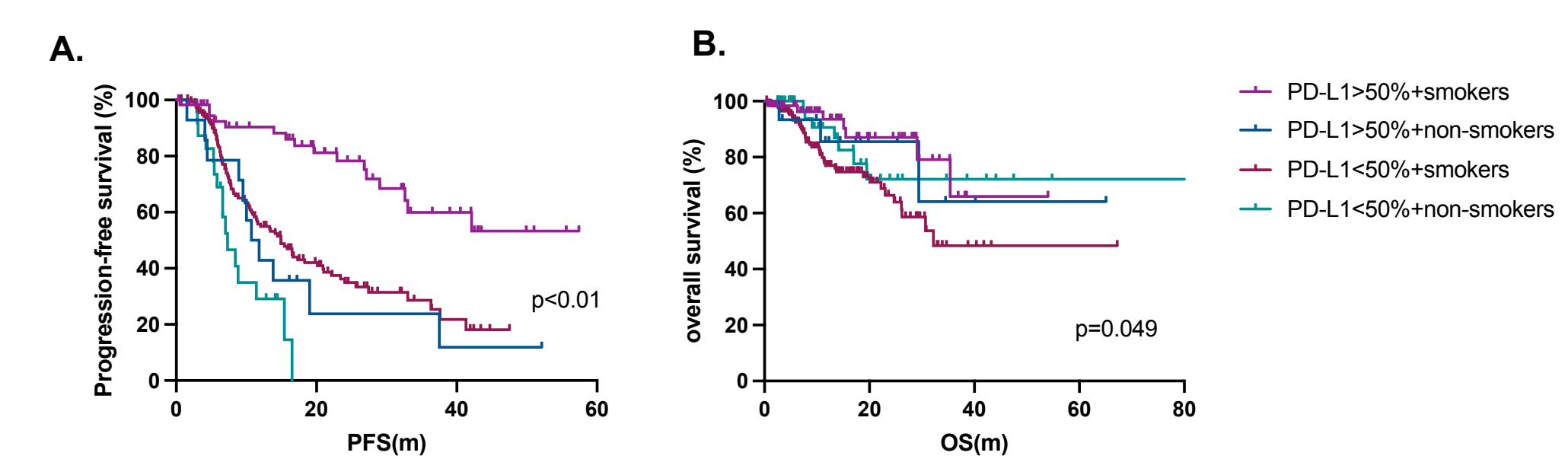


Figure 5. Association of combined PD-L1 expression and smoking status with PFS and OS among lung cancer patients treated with immunotherapy