

EP11.33: A real-world efficacy analysis of immune checkpoint inhibitor rechallenge in non-small cell lung cancer patients with postoperative recurrence



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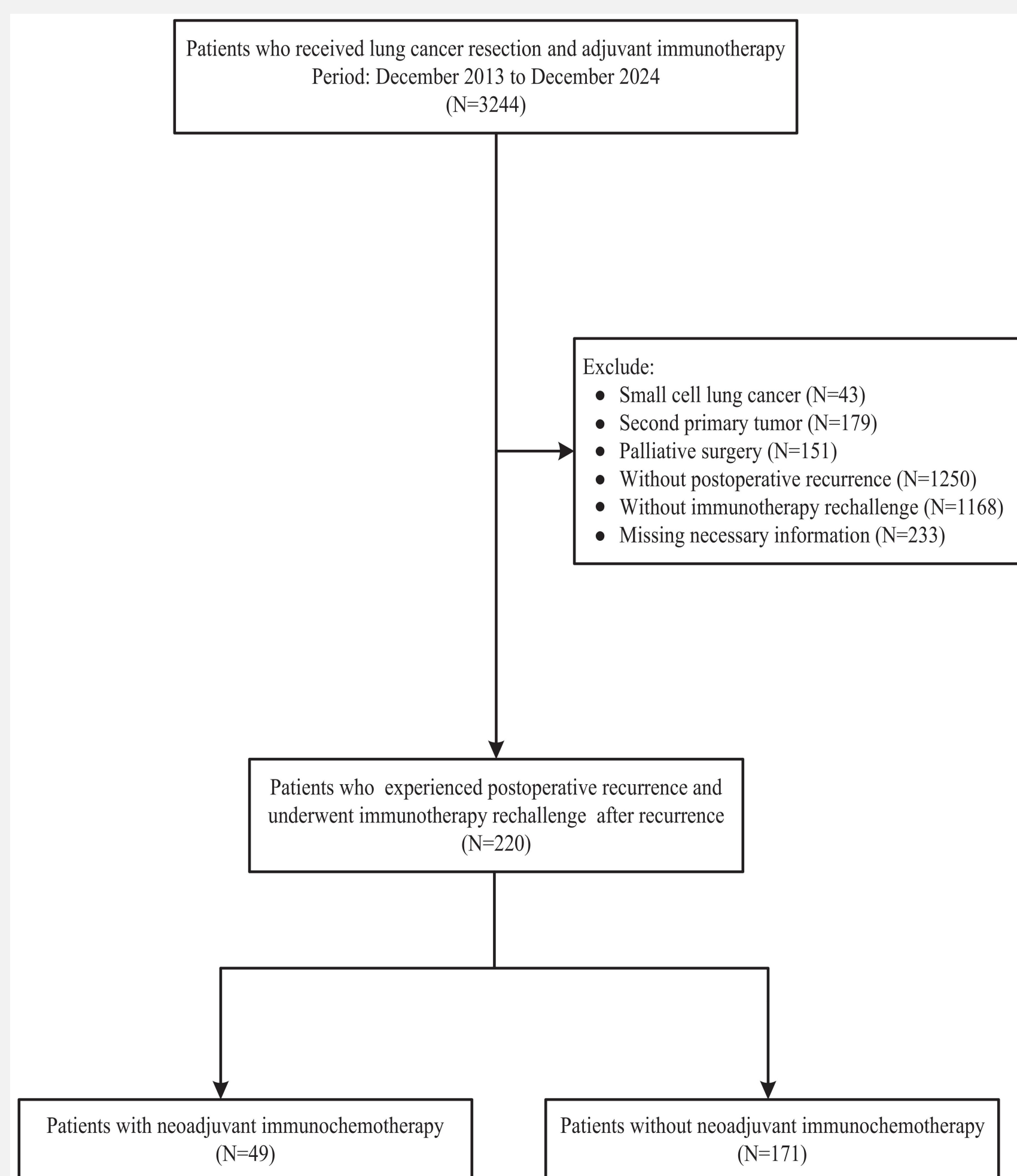
INTRODUCTION

◆ Immune-checkpoint inhibitors (ICIs) are currently the only widely used immunotherapies for patients with lung cancer. However, treatment options for patients with advanced-stage lung cancer who either have disease progression on ICIs or discontinue ICIs early in the course of treatment for other reasons, including irAEs, remain limited, with chemotherapy being one of the few standard-of-care approaches available for many patients. Encouragingly, emerging evidence indicates that some patients with advanced-stage cancers who previously received ICIs can derive benefit from ‘rechallenge’ with these agents.

◆ However, a set of accepted standard definitions and clinical management strategies for ICI rechallenge remains elusive. This study aimed to clarify the efficacy and safety of ICI rechallenge therapy in patients with NSCLC who experience postoperative recurrence. Additionally, we included the impact of ICI administration during the neoadjuvant therapy phase in our analysis.

METHODS

1. Patients enrollment and exclusion flowchart



2. This is a single-center, retrospective study involving patients who experienced recurrence following radical surgery and underwent ICI rechallenge treatment. Between December 2013 and December 2024, a total of 220 patients were finally included in this study. This study received approval from the Ethics Committee of Sun Yat-sen University Cancer Center (SL-B2025-656-01).

3. Clinical outcomes and statistic analysis:

- Progression-free survival (PFS1) was defined as the time from thoracic surgery to the first event of tumor progression, recurrence, or death.
- The PFS under rechallenge (PFS2) was defined as the time from the initiation of the rechallenge to the second disease progression, recurrence or death.
- PFS were evaluated using Kaplan-Meier analysis and Cox proportional hazards regression, with Maximally selected rank statistics employed to determined the optimal treatment interval.

RESULTS

Table 1. Baseline clinicopathological characteristics of patients received ICIs rechallenge

Table. Comparison of baseline characteristics of patients who experienced recurrence following radical surgery and underwent ICI rechallenge treatment				
Characteristics	Overall (N=220)	Without neoadjuvant immunotherapy (N=171)	With neoadjuvant immunotherapy (N=49)	P value*
Age, y, Median (IQR)	58.5 (53.0-65.0)	59.0 (53.0-65.0)	58.0 (52.0-63.0)	0.338
Sex, n (%)				0.311
Female	40 (18.2)	34 (19.9)	6 (12.2)	
Male	180 (81.8)	137 (80.1)	43 (87.8)	
Smoking, n (%)				0.234
No	81 (36.8)	67 (39.2)	14 (28.6)	
Yes/ever	139 (63.2)	104 (60.8)	35 (71.4)	
ECOG PS, n (%)				0.878
0	179 (81.4)	140 (81.9)	39 (79.6)	
1	41 (18.6)	31 (18.1)	10 (20.4)	
Peripheral tumor, n (%)				0.564
No	120 (54.5)	91 (53.2)	29 (59.2)	
Yes	100 (45.5)	80 (46.8)	20 (41.8)	
Location of the tumor, n (%)				0.552
Right upper lobe	55 (25.0)	42 (24.6)	13 (26.5)	
Right middle lobe	14 (6.4)	10 (5.8)	4 (8.2)	
Right lower lobe	45 (20.5)	34 (19.9)	11 (22.4)	
Left upper lobe	61 (27.7)	46 (26.9)	15 (30.6)	
Left lower lobe	45 (20.5)	39 (22.8)	6 (12.2)	
cT stage, n (%)				<0.001
T1-2	168 (76.4)	140 (81.9)	28 (57.1)	
T3-4	52 (23.6)	31 (18.1)	21 (42.9)	
cN stage, n (%)				<0.001
N0	98 (44.5)	89 (52.0)	9 (18.4)	
N1	33 (15.0)	24 (14.0)	19 (38.8)	
N2	65 (29.5)	54 (31.6)	11 (22.4)	
N3	14 (6.4)	4 (2.3)	10 (20.4)	
ypT stage, n (%)				<0.001
T0	13 (5.9)	/	13 (26.5)	
T1-2	180 (81.8)	154 (90.1)	26 (53.1)	
T3-4	27 (12.3)	17 (9.9)	10 (20.4)	
ypN stage, n (%)				0.538
N0	121 (55.0)	95 (55.6)	26 (53.1)	
N1	34 (15.5)	24 (14.0)	10 (20.4)	
N2	65 (29.5)	52 (30.4)	13 (26.5)	
Histologic type, n (%)				0.008
SCC	53 (24.1)	34 (19.9)	19 (38.8)	
ADC	115 (52.3)	98 (57.3)	17 (34.7)	

Others†	52 (23.6)	39 (22.8)	13 (26.5)	
Tumor differentiation degree, n (%)				<0.001
Well differentiation	29 (13.2)	7 (4.1)	22 (38.8)	
Moderately differentiated	112 (50.9)	86 (50.3)	26 (53.1)	
Poorly differentiated	76 (34.5)	75 (43.9)	1 (2.0)	
Undifferentiated	3 (1.4)	3 (1.8)	0	
PD-L1, n (%)				0.930
<1%	28 (12.7)	22 (10.0)	6 (12.2)	
1-50%	41 (18.6)	32 (14.5)	9 (18.4)	
≥50%	28 (12.7)	23 (10.5)	5 (10.2)	
Unknown	123 (55.9)	94 (42.7)	29 (59.2)	
Neoadjuvant cycles, n (%)				/
≤2	/	/	24 (49.0)	
3	/	/	12 (24.5)	
≥4	/	/	13 (26.5)	
Surgery, n (%)				0.039
Lobectomy	186 (84.5)	141 (82.5)	45 (91.8)	
Sublobar resection	24 (10.9)	23 (13.5)	1 (2.0)	
Pneumonectomy	10 (4.5)	7 (4.1)	3 (6.1)	
Surgical approach, n (%)				<0.001
VATS	158 (71.8)	139 (81.3)	19 (38.8)	
Open	62 (28.2)	32 (18.7)	30 (61.2)	
First recurrent site after surgery, n (%)				0.329
Distant	101 (45.9)	75 (43.9)	26 (53.1)	
Locoregional	119 (54.1)	96 (56.1)	23 (46.9)	
Local	52 (23.6)	44 (25.7)	8 (16.3)	
Rechallenge intervals, m, Median (IQR)	3.5 (2.5-6.5)	3.0 (2.0-5.5)	5.5 (3.0-11.5)	0.002

Figure 1. Kaplan-Meier curves stratified by irAEs for PFS2

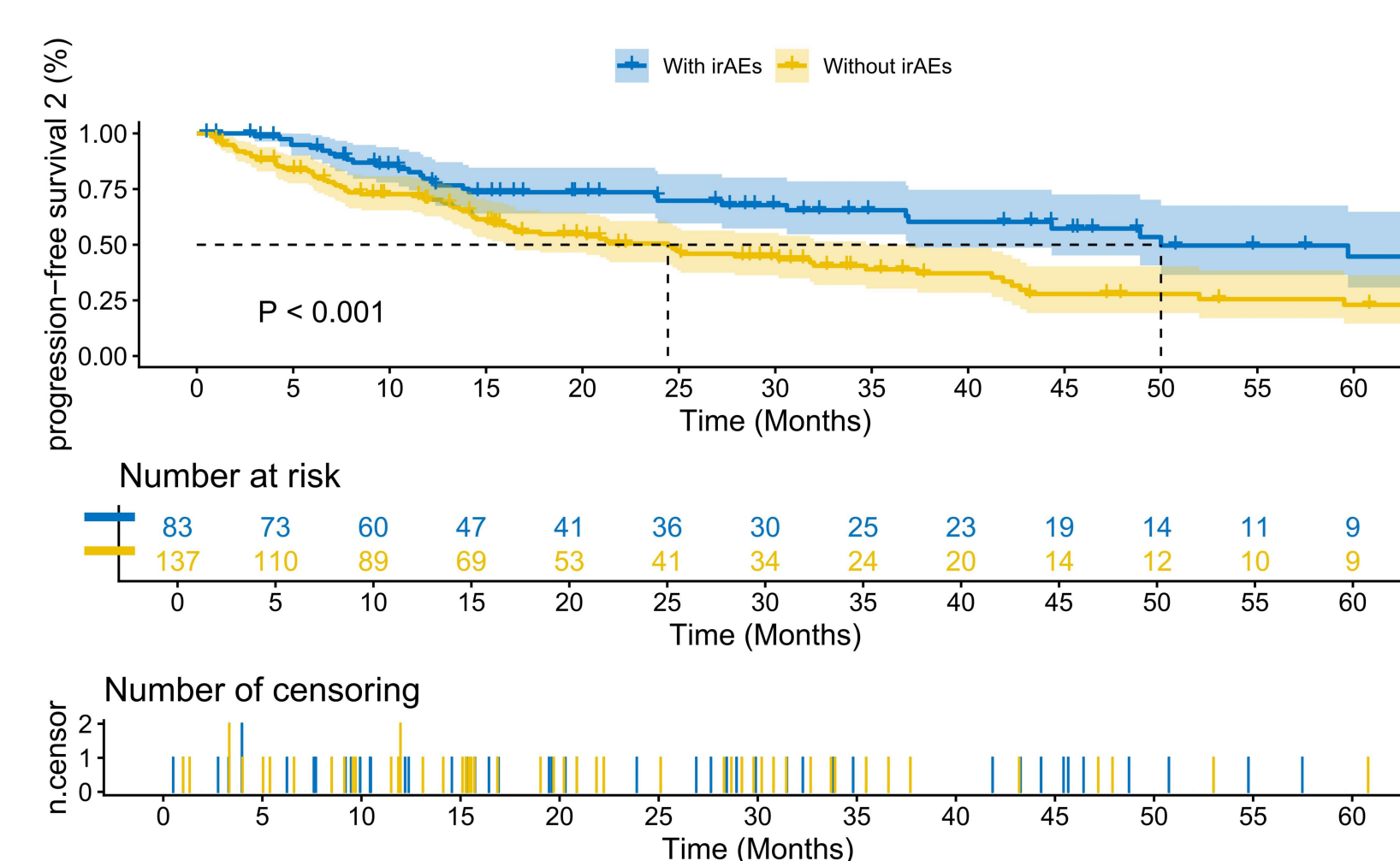


Figure 2. Kaplan-Meier curves stratified by 4 metastatic sites for PFS2

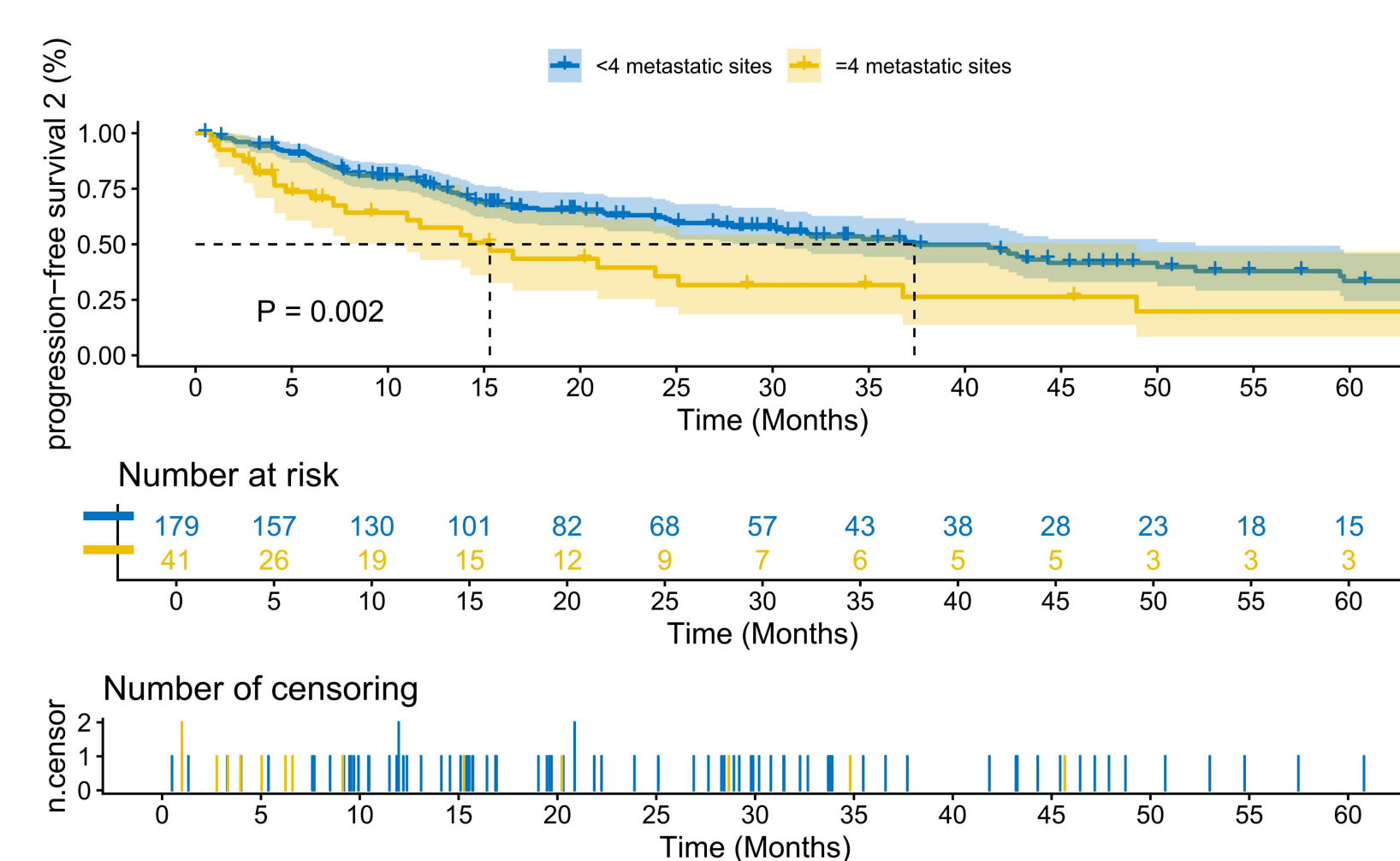
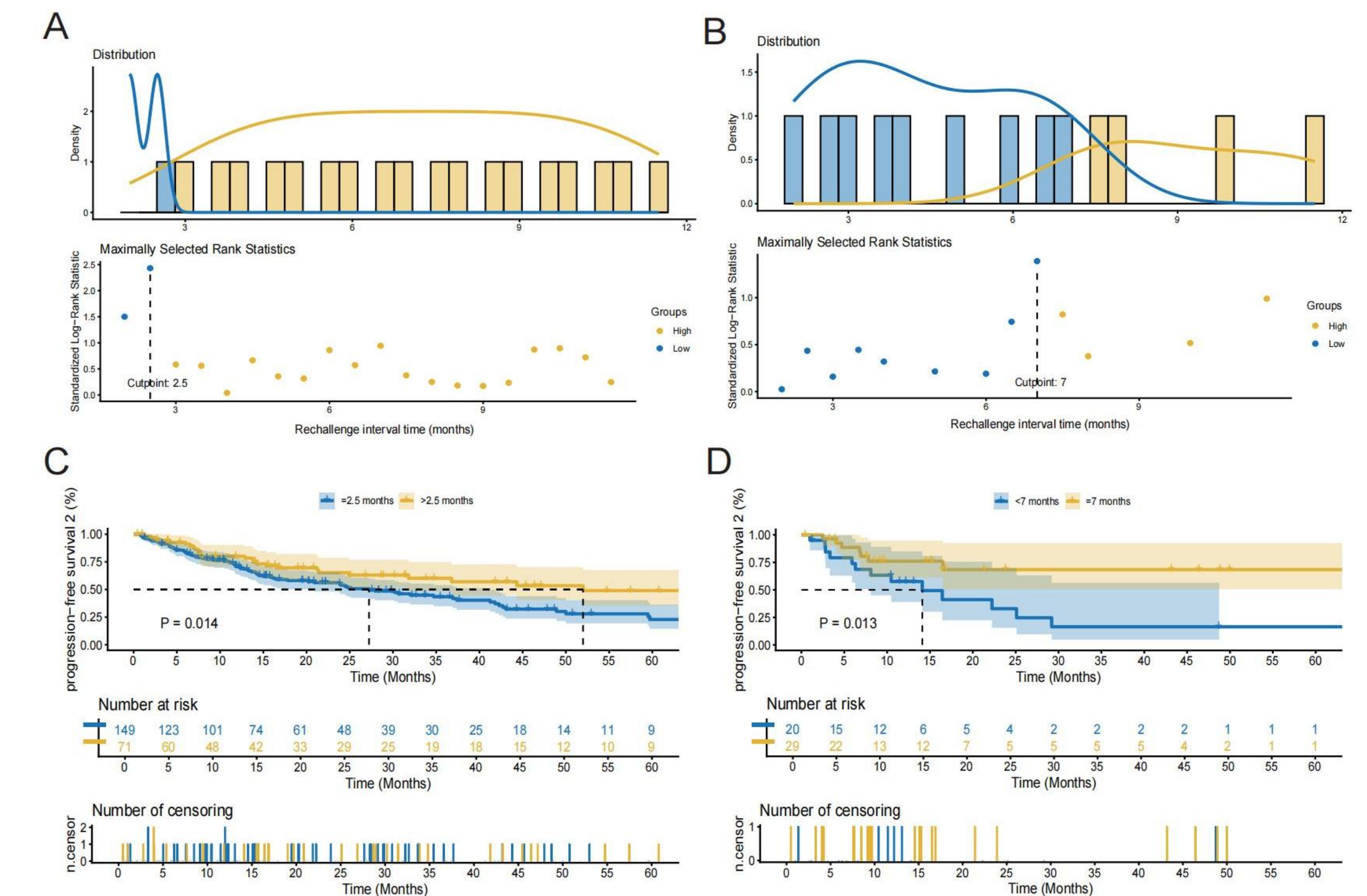


Figure 3. Optimal interval time of rechallenge calculated by maximally selected rank statistic in the cohort with and without neoadjuvant immunotherapy.



DISCUSSION AND CONCLUSION

◆ At present, the ICIs rechallenge in lung cancer is usually defined as repeat treatment with an ICI of the same class after a period of treatment discontinuation (owing to disease progression or irAEs). Some reviews suggested that ICI rechallenge is a valuable intervention in selected patients with advanced-stage NSCLC. In comparison to the other available options for most patients, ICI rechallenge offers the possibility of long-term disease regression, often with fewer adverse events.

◆ ICIs are generally better tolerated than chemotherapy, although these agents can cause irAEs, except for a few events of grade ≥3 severity, these are usually reversible. In addition, although many patients do not derive durable benefit from these agents, a subset of patients with a response to ICIs has been shown to have long-lasting off-treatment remissions.

◆ In our cohort, ICI rechallenge presented a viable treatment option for postoperative recurrence of NSCLC, especially recommended for those with irAEs and <4 metastatic sites. An interval of >2.5 months for rechallenge may be more appropriate, while this interval should be extended to 7 months in neoadjuvant immunotherapy group.

REFERENCES & ACKNOWLEDGEMENTS

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