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Timing of Immune Checkpoint Inhibitor Administration in Resected NSCLC Receiving Adjuvant Therapy

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Disclosure

COI

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I have no relevant financial relationships to disclose.

Disclosure

Artificial Intelligence (AI) Use Disclaimer

AI tool used: ChatGPT (OpenAI) was used for English-language editing and assistance with slide and figure preparation. All scientific content, data, statistical analyses, and interpretations were independently reviewed and verified by the authors.

Relationship Between Immune Function and Circadian Rhythms

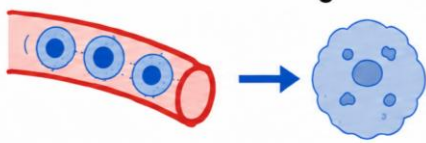
- Immune cell function and trafficking are regulated by circadian rhythms.
- In particular, the function and trafficking of **CD8⁺ T cells**, a major target of ICIs, exhibit diurnal variations.
- Antigen recognition and elimination have been reported to be more effective in the early morning.

T-cell Function



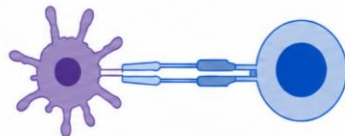
Varies by Time of Day

Immune Cell Circulation and Trafficking



Changes Over Time

Antigen Recognition and Immune Response



Efficiency Varies by Time of Day

↓
The timing of ICI administration may influence treatment efficacy.

Karaboue A, et al. *Cancers*. 2022;14:896.

Background

A retrospective study of patients with locally advanced NSCLC reported that later durvalumab administration was significantly associated with shorter PFS. (Patients receiving $\geq 20\%$ of durvalumab infusions after 3:00 PM had significantly shorter PFS.)

Hirata T, et al. JTO Clin Res Rep. 2024;5:100659.



However, the association between ICI administration timing and clinical outcomes in the adjuvant setting remains insufficiently investigated.

Study Objective

To investigate the association between the timing of adjuvant ICI administration and clinical outcomes after surgery.

Methods

- We retrospectively analyzed **27 patients with NSCLC** who received at least one cycle of postoperative adjuvant ICI therapy at our institution between January 2022 and April 2026, excluding patients who were still receiving treatment.
- Patients were classified into two groups according to the proportion of treatment cycles initiated by 3:00 PM:
 - **Early group:** $\geq 50\%$ of cycles initiated by 3:00 PM (n = 17)
 - **Late group:** $< 50\%$ of cycles initiated by 3:00 PM (n = 10)
→ RFS and OS were compared between the two groups.

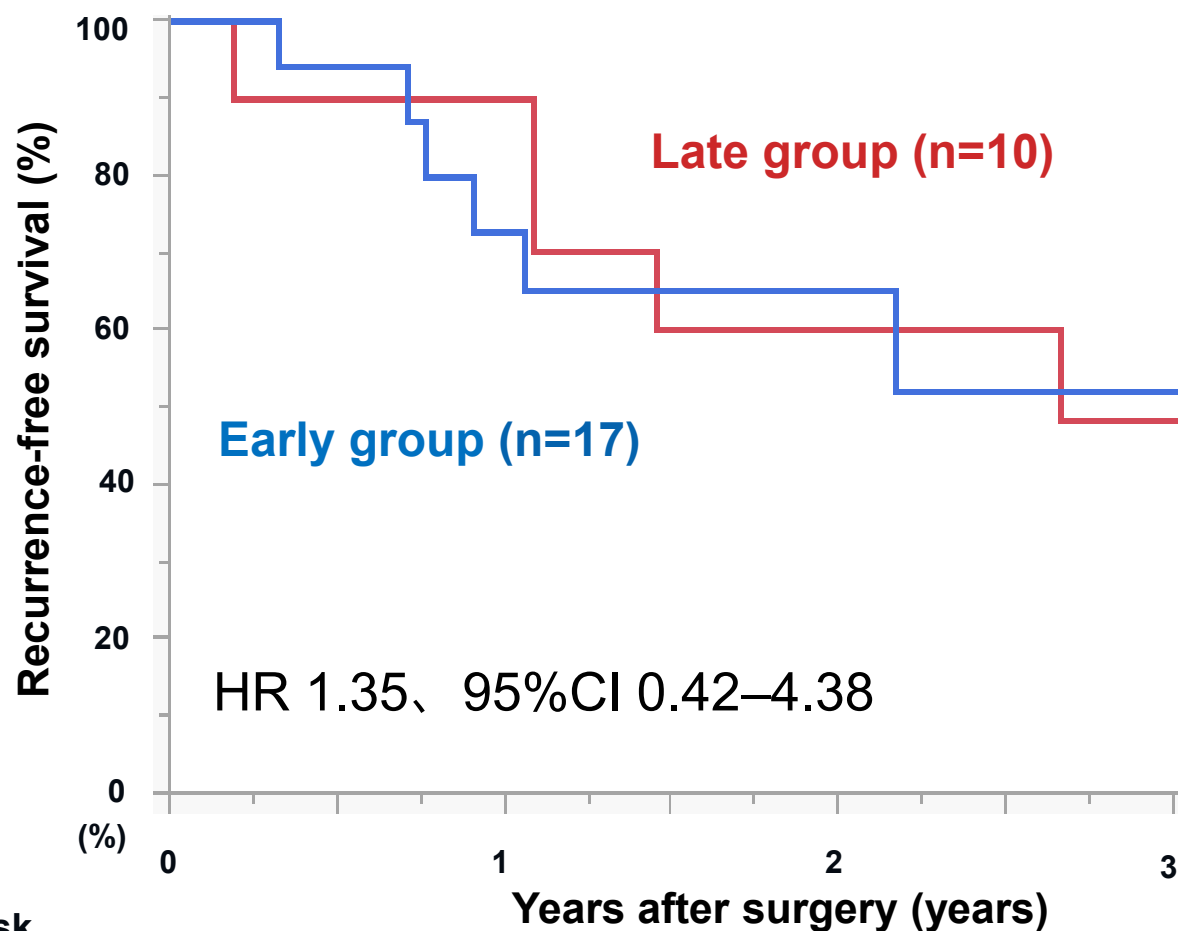
Patient Characteristics

Early group: $\geq 50\%$ of ICI cycles initiated by 3:00 PM

Late group: $< 50\%$ of ICI cycles initiated by 3:00 PM

Variables	Overall (n = 27)	Early group (n = 17)	Late group (n = 10)	P-value
Age, years(Median)	72 (67-76)	75 (66-77)	69 (66-73)	0.905
Sex, male/female	20(74%)/7(26%)	14(82%)/3(18%)	6(60%)/4(40%)	0.365
Smoking, yes	24(89%)	15(88%)	9(90%)	>0.999
Pathological stage, Stagelll	11 (41%)	6 (35%)	5 (50%)	0.687
Histology, Sq	7 (26%)	4 (24%)	3 (30%)	>0.999
PD-L1, $\geq 50\%$	17 (63%)	9 (53%)	8 (80%)	0.338
Number of chemotherapy cycles(Median)	1 (1-3)	1 (1-4)	1 (1-2)	0.275
Number of ICI cycles(Median)	13 (7-16)	13 (9-16)	12 (3-16)	0.294
Immune-related adverse events	9 (33)	5 (29)	4 (40)	0.683

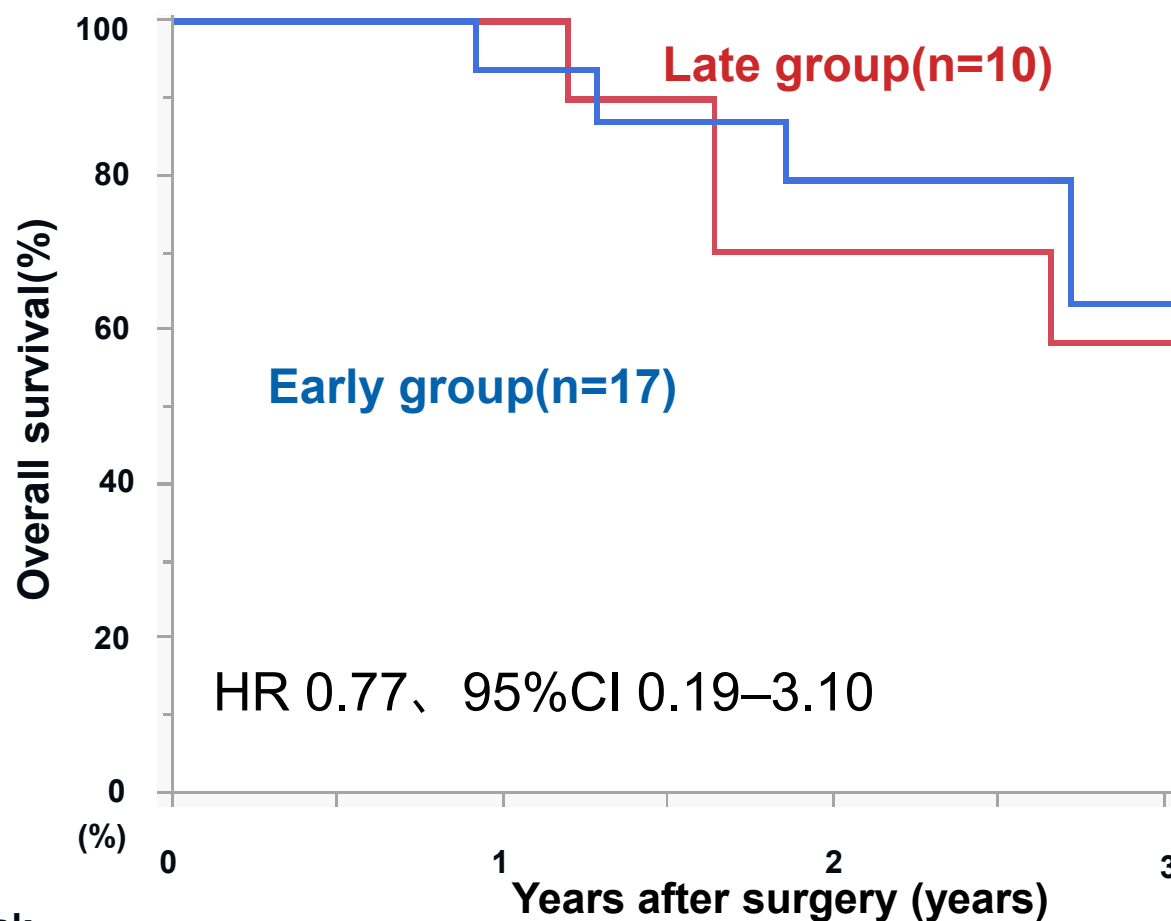
Recurrence-free survival



No significant difference in RFS was observed between the two groups.

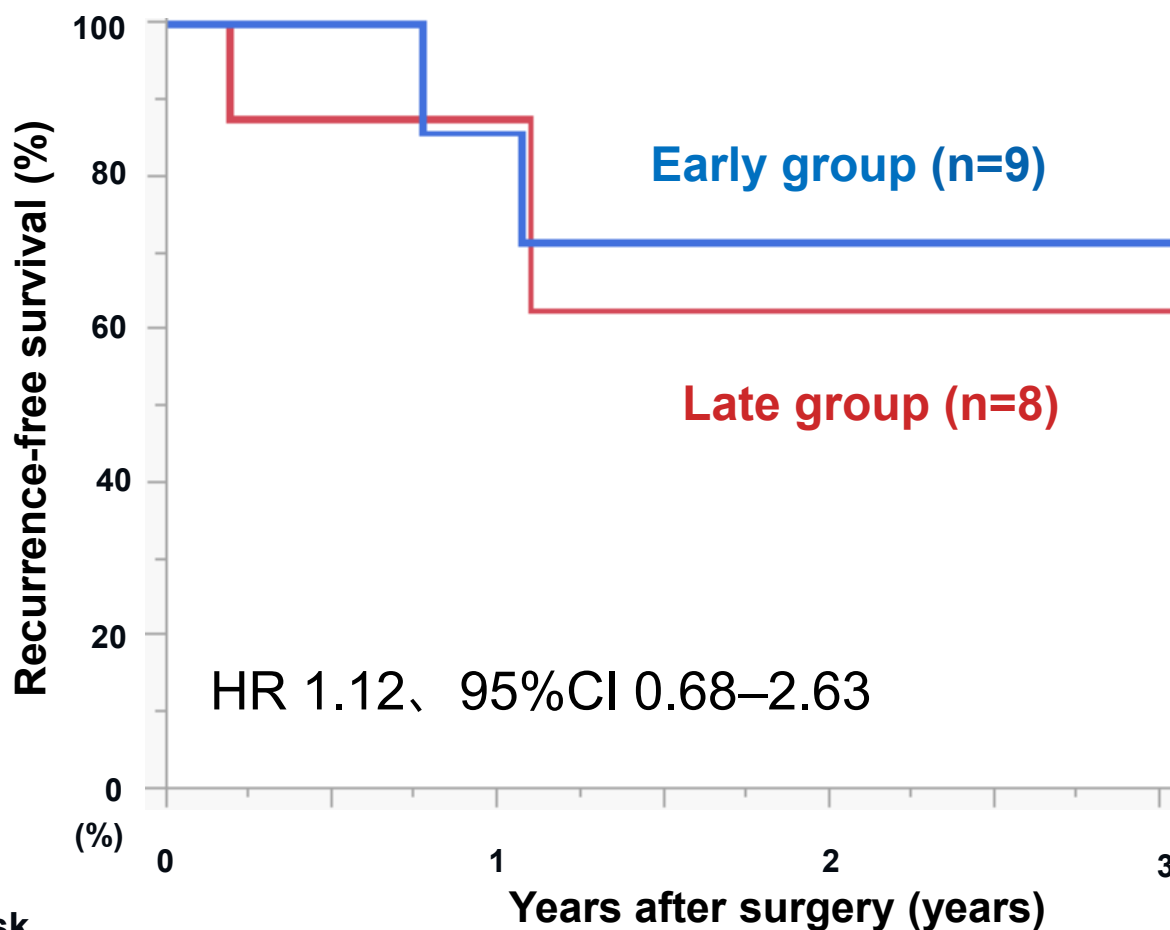
≥50% of cycles initiated by 3:00 PM 17
<50% of cycles initiated by 3:00 PM 10

Overall survival



No significant difference in OS was observed between the two groups.

Recurrence-free survival in PD-L1 $\geq$ 50%

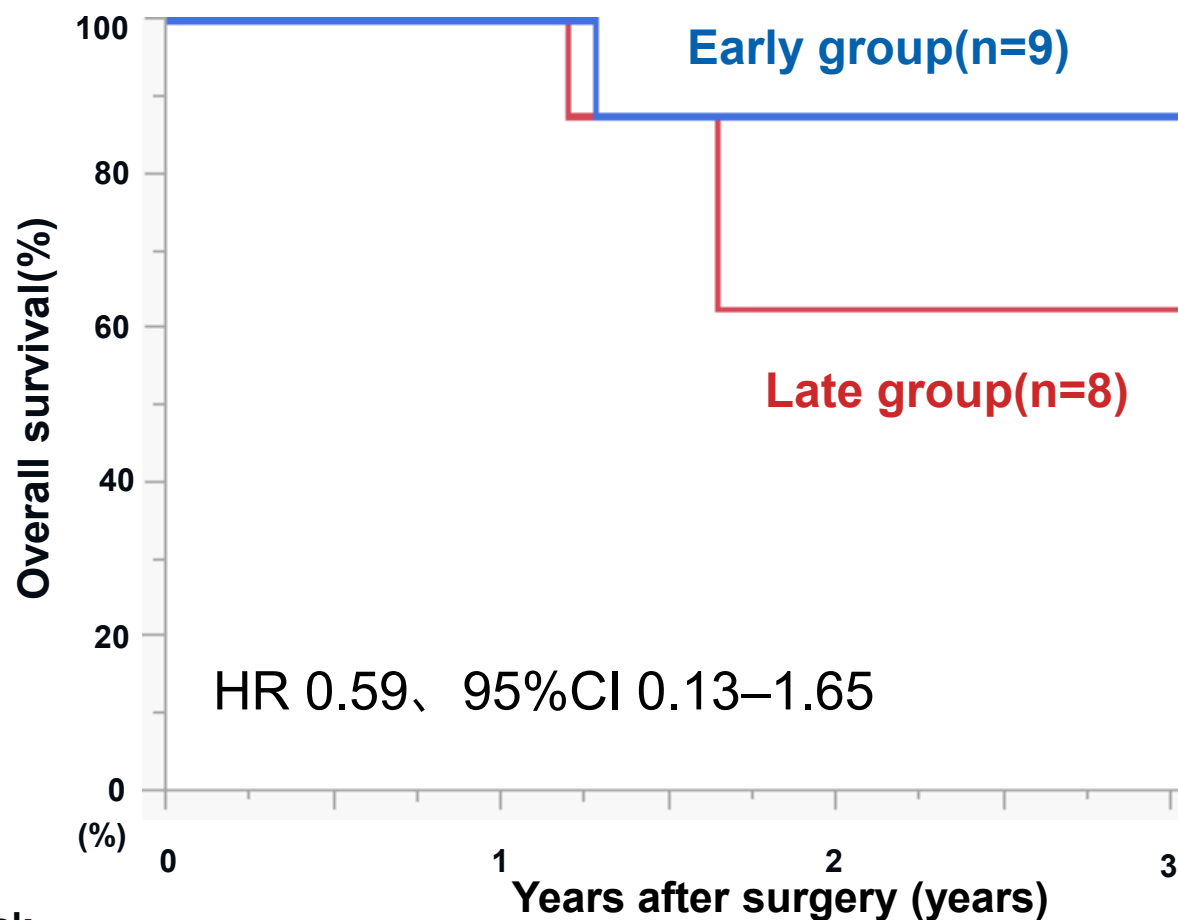


No significant difference in RFS was observed between the two groups.

Number at risk

	0	1	2	3
≥50% of cycles initiated by 3:00 PM	9	7	4	3
<50% of cycles initiated by 3:00 PM	8	8	5	5

Overall survival in PD-L1 $\geq$ 50%



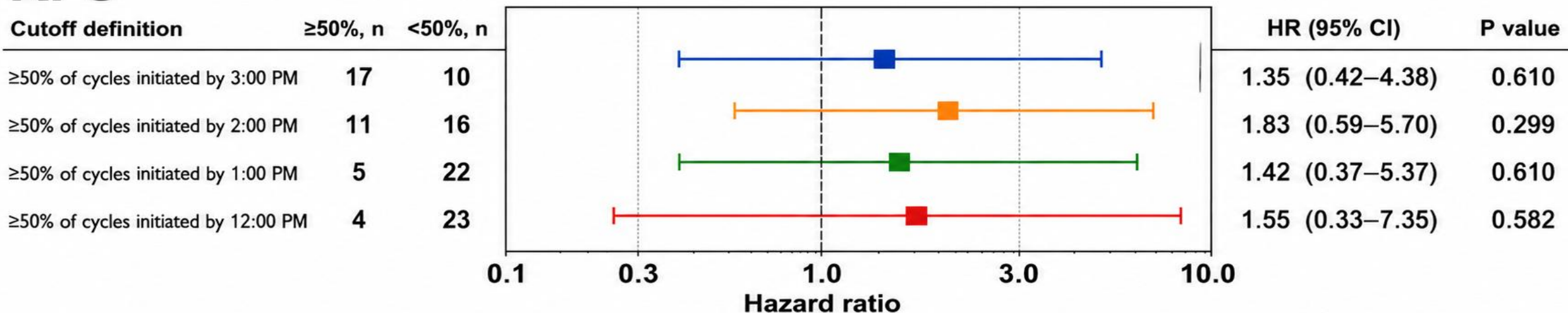
No significant difference in OS was observed between the two groups.

Number at risk

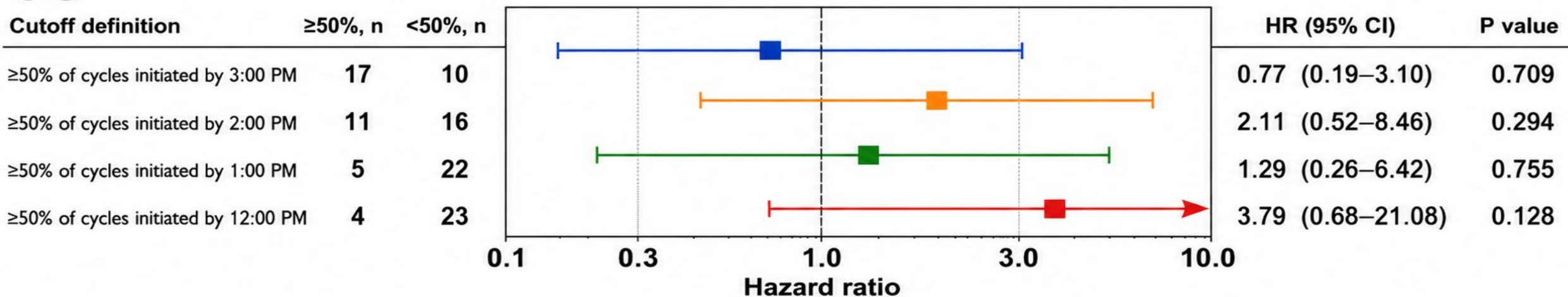
	0	1	2	3
$\geq 50\%$ of cycles initiated by 3:00 PM	9	9	6	3
$< 50\%$ of cycles initiated by 3:00 PM	8	8	5	5

Sensitivity Analyses Using Alternative Cutoff Times

RFS



OS



Cox Regression Analysis for RFS

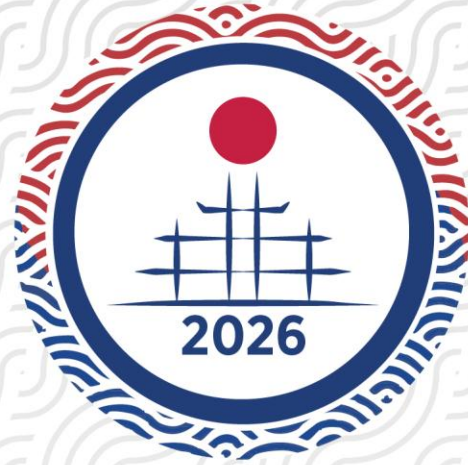
Factor	Univariable		Multivariable	
	HR (95%CI)	P value	HR (95%CI)	P value
Age (≥ 70 vs. < 70 years)	1.27 (0.71-2.33)	0.418		
Sex (male vs. female)	0.47 (0.15-1.51)	0.207		
Smoking history (yes vs. no)	0.82 (0.18-3.86)	0.803		
Pathological stage (III vs. II)	0.87 (0.27-2.78)	0.808		
Histology (squamous vs. non-squamous)	0.50 (0.11-2.31)	0.373		
PD-L1 expression ($\geq 50\%$ vs. $< 50\%$)	0.39 (0.12-1.31)	0.130	0.41(0.12-1.38)	0.148
ICI administration timing (late vs. early)	1.35 (0.41-4.38)	0.613	1.16 (0.34–3.88)	0.814

Cox Regression Analysis for OS

Factor	Univariable		Multivariable	
	HR (95%CI)	P value	HR (95%CI)	P value
Age (≥ 70 vs. < 70 years)	0.49 (0.12-2.06)	0.331		
Sex (male vs. female)	0.17 (0.04-0.70)	<u>0.015</u>	0.17 (0.04–0.71)	<u>0.016</u>
Smoking history (yes vs. no)	0.41 (0.08-2.05)	0.275		
Pathological stage (III vs. II)	0.70 (0.16-2.96)	0.627		
Histology (squamous vs. non-squamous)	0.33 (0.04-2.68)	0.373		
PD-L1 expression ($\geq 50\%$ vs. $< 50\%$)	0.57 (0.14-2.27)	0.422		
ICI administration timing (late vs. early)	0.77 (0.19-3.10)	0.709	0.99 (0.24–4.04)	0.987

Conclusions

- **The timing of ICI administration in the postoperative adjuvant setting was not significantly associated with RFS or OS.**
- **Given the retrospective, single-center design of this study, these findings should be validated in larger, multicenter cohorts.**



Thank You.