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INTRODUCTION

- Lung cancer is the leading cause of cancer-related death worldwide, with a 5-year survival rate of 5.8% among patients diagnosed with metastatic non-small cell lung cancer (NSCLC).¹⁻³
- Immune checkpoint inhibitors (ICIs) have improved 5-year survival rates in patients with NSCLC to 15-32%, although response rates vary by patient and tumor characteristics.^{1, 4-5}
- Emerging evidence suggests that patient responses to ICIs may depend on the time of day (ToD) of administration, indicating that optimizing ICI timing could improve outcomes, although no formal recommendations exist.

OBJECTIVES

- Evaluate current patterns of ToD administration of ICIs at a large multi-site community cancer center.
- Evaluate whether clinical benefit (OS, PFS) varies according to ToD in which ICI is administered in patients with metastatic NSCLC.
- Describe the incidence and pattern of immune-related adverse events (irAEs) according to ToD of ICI administration.

METHODS

Single-center retrospective chart review conducted between January 1st, 2021 and December 31st, 2024 at Memorial Cancer Institute (MCI).

PFS was determined by treating-physician's assessment and graded using RECIST v1.1 criteria. Approved by the Memorial Healthcare System Institutional Review Board.

Patient Population

- Adults aged 18 years or older
- Advanced NSCLC receiving frontline chemo-immunotherapy (carboplatin/pemetrexed/pembrolizumab)

Statistical Methods

- Descriptive statistics: patient demographics, time of ICI administration, time to disease progression, time to death, and incidence of irAEs
- Continuous variables: means with SD or medians with range; categorical variables: frequencies and percentages
- Kaplan-Meier method used to estimate median OS and PFS; groups compared using the log-rank test
- No adjustment was made for multiple comparisons or for baseline covariates and duration of ICI exposure; reported p-values are nominal

RESULTS

Table 1. Patient Baseline Characteristics

Characteristics	Early (n=36)	Late (n=46)
Median age (range) - yr	65.5 (47-81)	70.7 (41-87)
Sex – no (%)		
Male	22 (61.1%)	22 (47.8%)
ECOG Status – no (%)		
0	28 (77.8%)	33 (71.7%)
1	6 (16.7%)	8 (17.4%)
2	1 (2.8%)	4 (8.7%)
3	1 (2.8%)	0 (0.0%)
4	0 (0.0%)	1 (2.2%)
Race – no (%)		
White Caucasian	20 (55.6%)	22 (47.8%)
African American or Black	7 (19.4%)	9 (19.6%)
Hispanic	8 (22.2%)	13 (28.3%)
Asian	0 (0.0%)	1 (2.2%)
Middle Eastern	1 (2.8%)	1 (2.2%)
PD-L1 Status		
<1%	16 (44.4%)	20 (43.5%)
1-49%	9 (25.0%)	7 (15.2%)
>50%	7 (19.4%)	8 (17.4%)
Unknown	4 (11.1%)	11 (23.9%)
Smoking History		
Yes	32 (88.9%)	40 (87.0%)
No	4 (11.1%)	6 (13.0%)

Figure 1. Overall Survival.

Interpretation. longer median OS with early-day dosing (21 vs 16 mo); not significant (p=0.376).

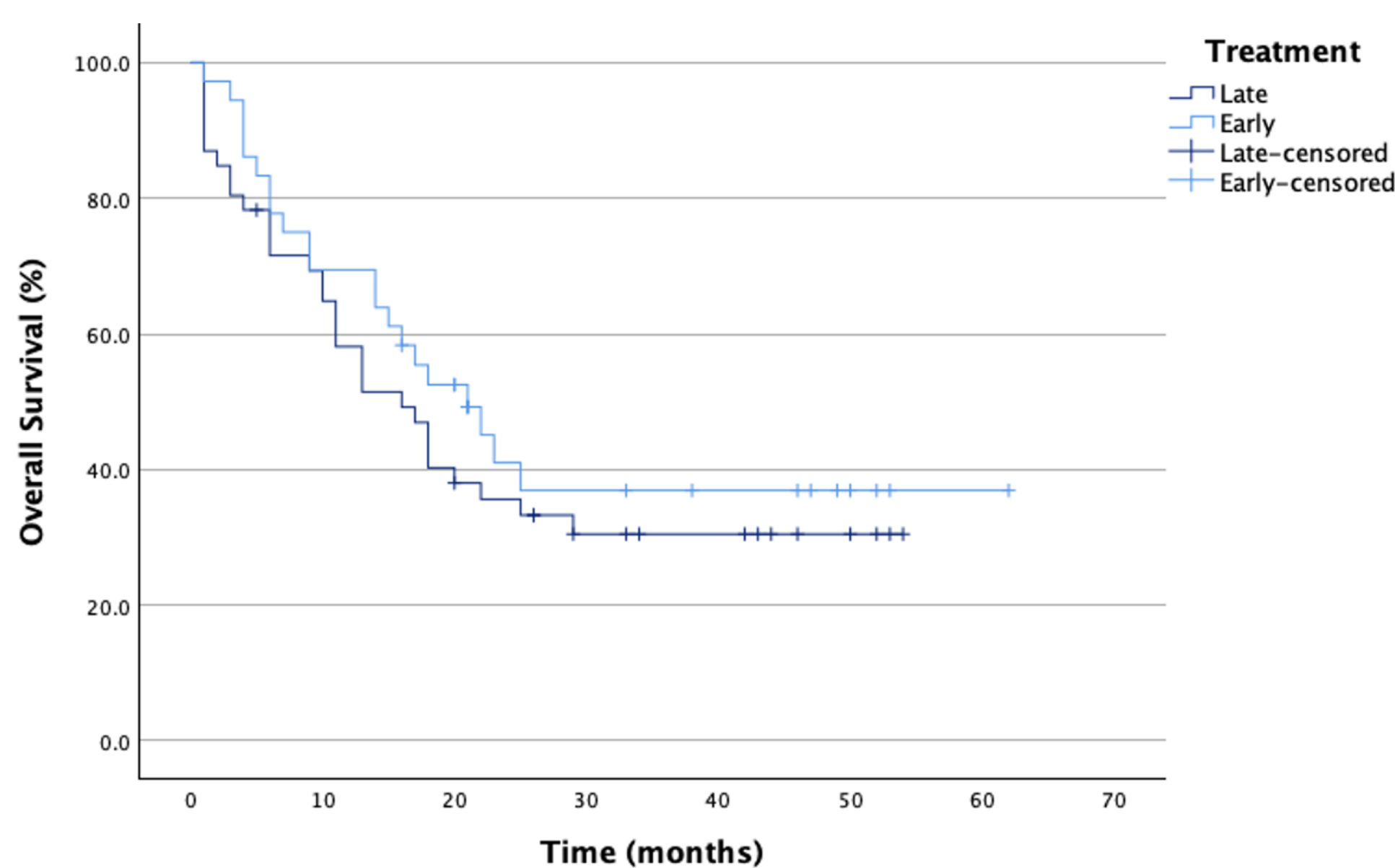


Figure 3. Incidence of irAEs

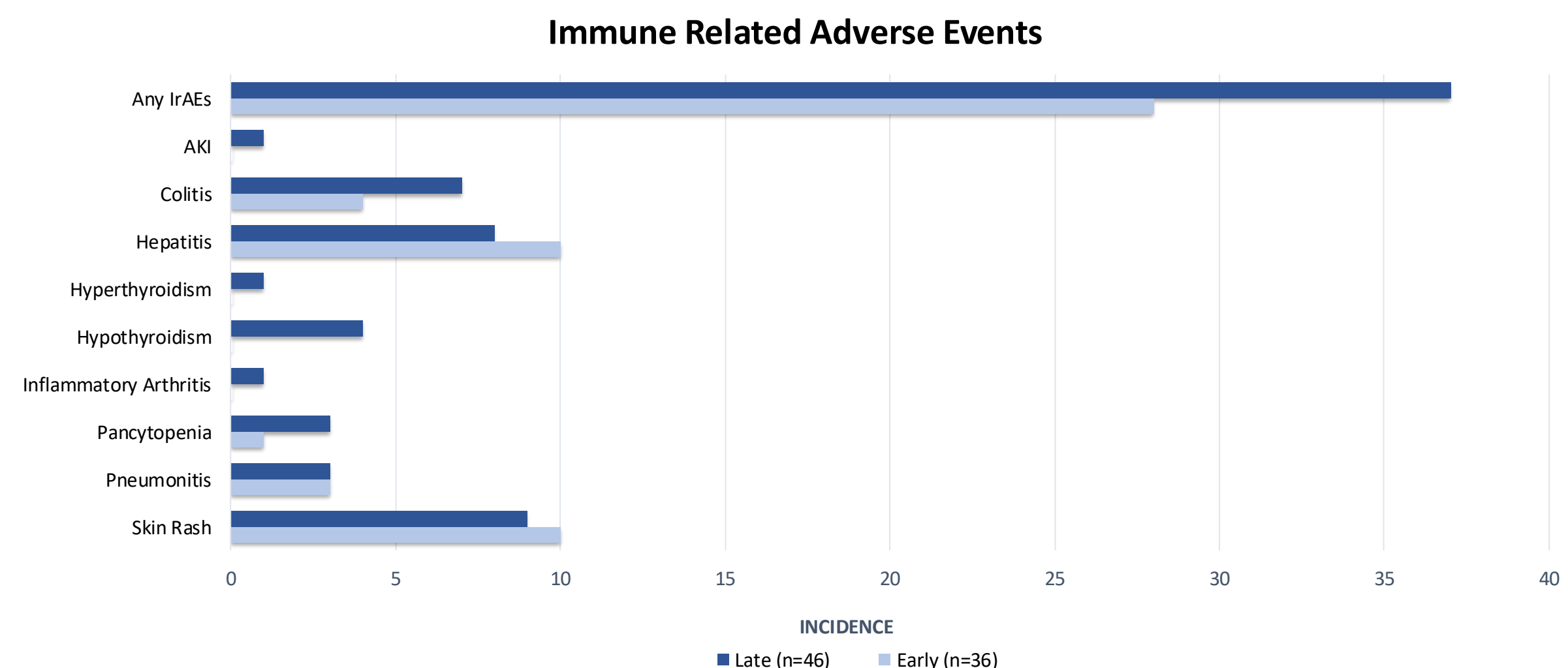


Table 2. Time-of-Day Administration (All Indications)

Defined Cut-Off	Number of Doses	Percentage
Before 12:00 PM	6,969	50.1%
After 12:00 PM	6,939	49.9%

ICI administration timing was evenly distributed across the health system

Table 3. Time-of-Day Administration (Study Cohort)

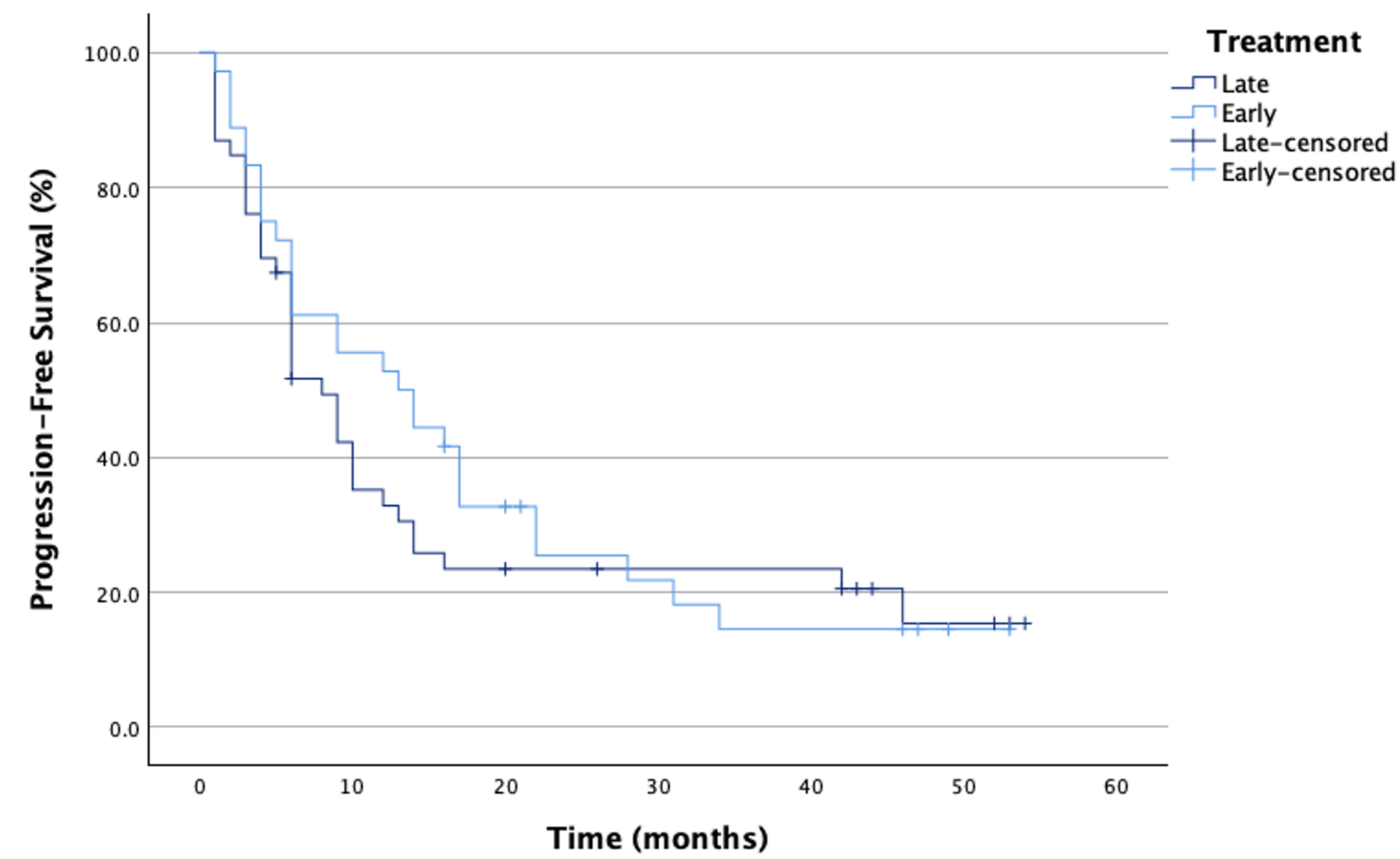
Defined Cut-Off	Number of Patients	Percentage
Before 12:00 PM	36	44%
After 12:00 PM	46	56%

Table 4. Final Survival Summary

Group	Median OS, mo (95% CI)	Median PFS, mo (95% CI)
Early ToD	21.0 (14.1-27.9)	13.0 (5.7-20.4)
Late ToD	16.0 (10.3-21.7)	8.0 (5.7-10.3)
Overall	18.0 (13.2-22.8)	9.0 (5.2-12.8)

Figure 2. Progression-Free Survival.

Interpretation. longer median PFS with early-day dosing (13 vs 8 mo); not significant (p=0.476).



LIMITATIONS

- Single-institution, retrospective cohort (n=82); limited power and event count.
- Unadjusted analyses; residual confounding cannot be excluded.
- Time-of-day reflects infusion scheduling, not randomization.
- Limited follow-up yields immature OS estimates.
- Progression and irAEs investigator-assessed by chart review.
- Hypothesis-generating; prospective validation warranted.

DISCUSSION & CONCLUSION

- In this real-world analysis of patients receiving immunotherapy, infusion timing was nearly equally distributed across all indications and immune checkpoint inhibitors (50.1% early vs 49.9% late).
- In the cohort of patients with metastatic NSCLC receiving frontline chemo-immunotherapy, infusion timing was broadly split across the treatment day (44% early vs 56% late), reflecting scheduling practice rather than clinical intent.
- Early-day administration was associated with numerically longer median OS (21 vs 16 months) and PFS (13 vs 8 months). Neither difference reached statistical significance and the confidence intervals overlapped, consistent with a limited sample size and event count.
- The direction of effect is concordant with prior chronotherapy analyses in NSCLC and melanoma, which have reported improved survival when immune checkpoint inhibitors are infused earlier in the day.
- Safety profiles were comparable between groups, with no signal of increased immune-related adverse events with early-day infusion. These differences were not analyzed for statistical significance.
- No standardized recommendation for time-of-day dosing exists in current NCCN or ESMO guidance, and infusion scheduling remains driven by clinic capacity and patient preference.

Conclusion: Time of day is a modifiable, no-cost variable in ICI therapy. This hypothesis-generating, real-world study supports early-day administration as a candidate strategy and warrants validation in larger multicenter cohorts with multivariable adjustment, and ultimately in a prospective randomized study.

REFERENCES & DISCLOSURES

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- Kyra Thompson is supported by a Bristol Myers Squibb (BMS)-funded oncology residency.
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Scan here for references and team details



Abbreviations: CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; ESMO, European Society for Medical Oncology; ICI, immune checkpoint inhibitor; irAE, immune-related adverse event; IRB, Institutional Review Board; MCI, Memorial Cancer Institute; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; SD, standard deviation; ToD, time of day.