

P1.333: Association of Chemoimmunotherapy Completion Timing with Survival in Stage IV Non-Small Cell Lung Cancer



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Background

- Circadian rhythms may influence antitumor immunity and treatment response.¹
- Prior retrospective studies have suggested improved outcomes with earlier immune checkpoint inhibitor administration.²
- We evaluated the association between time-of-day (ToDA) of chemoimmunotherapy completion and survival outcomes in a real-world metastatic non-small cell lung cancer (NSCLC) cohort.

Methods

- Retrospective single-institution study at Levine Cancer Institute.
- Included adults aged 18 years or older with stage IV NSCLC, who initiated first-line pembrolizumab plus platinum-based chemotherapy between April 2022 and March 2024.
- Eligible regimens included carboplatin / pemetrexed, carboplatin / paclitaxel, and carboplatin / nab-paclitaxel.
- Total cohort: N = 157.
- ToDA was classified using treatment completion times from the first 4 courses:
 - Early ToDA was >50% of treatments completed before 15:00
 - Late ToDA was >50% of treatments completed after 15:00
- Primary outcomes were progression-free survival (PFS) and overall survival (OS).
- Survival was evaluated using Kaplan-Meier estimates, log-rank testing, and Cox proportional hazards models. Multivariable models adjusted for available demographic and clinical covariates. Adjusted survival curves were generated using direct adjustment.

157 patients

Early ToDA

n = 103

> 50% of completions before 15:00

Late ToDA

n = 54

> 50% of completions after 15:00

Baseline Characteristics

- Most baseline clinical characteristics were similar between cohorts.
- However, Late ToDA included more squamous histology (44.4% vs 15.5%; $p < 0.001$), greater paclitaxel use (44.4% vs 2.9%; $p < 0.001$), and a different race distribution ($p = 0.044$) including a higher proportion of African American patients (38.9% vs 20.4%).
- PD-L1 expression and distribution of metastatic disease were otherwise similar between cohorts.

Survival Analyses

KEY FINDING

Later chemoimmunotherapy completion was independently associated with significantly improved adjusted PFS and OS

- ✓ 53% lower adjusted hazard of progression or death (PFS)
- ✓ 52% lower adjusted hazard of death (OS)

Figure 1. Adjusted PFS by Timing of Chemoimmunotherapy Completion

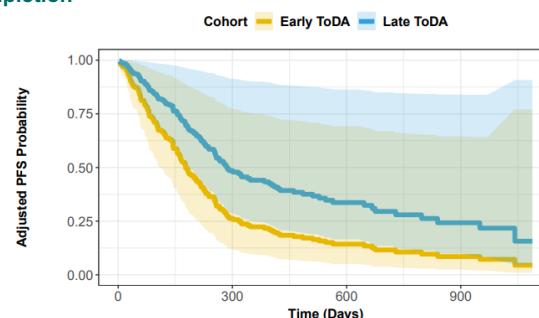
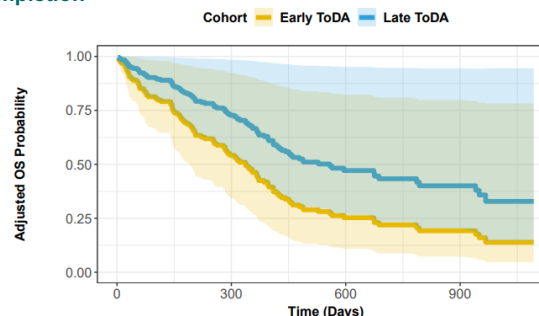


Figure 2. Adjusted OS by Timing of Chemoimmunotherapy Completion



Key Outcomes Summary

Outcome	Early ToDA (n = 103)	Late ToDA (n = 54)
PFS events, n (%)	88 (85.4%)	39 (72.2%)
Median PFS, days (95% CI)	198 (159-251)	218 (177-511)
Adjusted median PFS, days	177	287
Adjusted PFS HR (95% CI)	Reference	0.47 (0.28–0.81), p = 0.007
OS events, n (%)	74 (71.8%)	32 (59.3%)
Median OS, days (95% CI)	354 (291-410)	478 (338-NA)
Adjusted median OS, days	338	558
Adjusted OS HR (95% CI)	Reference	0.48 (0.26–0.89), p = 0.019

Interpretation and Conclusions

- In this real-world cohort of patients with stage IV NSCLC receiving first-line pembrolizumab-based chemoimmunotherapy, later treatment completion was independently associated with improved PFS and OS after multivariable adjustment.
- These findings contrast with prior reports suggesting improved outcomes with earlier ICI administration and highlight the complexity of treatment-timing effects with chemoimmunotherapy.
- Potential explanations for these contrasting findings include population- and geography-related differences in circadian biology and regimen-specific effects of treatment timing on chemotherapy and antitumor immunity, which warrant further investigation.
- Prospective validation is needed before treatment timing can be incorporated into clinical practice. If confirmed, timing-based scheduling could represent a pragmatic, low-cost strategy to optimize chemoimmunotherapy delivery.

References and Acknowledgements

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