Association Between Time of Day of Induction Immune Checkpoint Inhibitor Administration and Clinical Outcomes in Cutaneous Melanoma: A Propensity Score Matched Real-World Analysis

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INTRODUCTION

- Immune checkpoint inhibitors (ICIs) have transformed the treatment of cutaneous melanoma across all disease settings.
- Emerging data suggest that circadian biology may influence antitumor immune responses and potentially modify the efficacy and toxicity of immunotherapy. However, chronotherapy studies have reported inconsistent findings, and the clinical relevance of routine infusion timing remains uncertain.
- We evaluated whether the timing of induction immunotherapy administration was associated with survival outcomes and immune-related adverse events in a real-world cutaneous melanoma cohort.

METHODS

- Retrospective cohort study of patients with melanoma treated ICIs
- Patients were categorized as receiving early or late treatment based on average infusion time during induction immunotherapy. Early treatment was defined as an average induction infusion time before 12:00 PM.
- Propensity score matching was performed using age, race, sex, ECOG performance status, academic versus community treatment site, smoking history, aMnd melanoma stage.
- OS, PFS, and irAEs were compared between early and late treatment groups.
- Additional analyses were performed among patients with advanced unresectable/metastatic melanoma.

Hypothesis

- Circadian timing of immune checkpoint inhibitor administration may influence survival outcomes and immune-related toxicity in patients with melanoma.

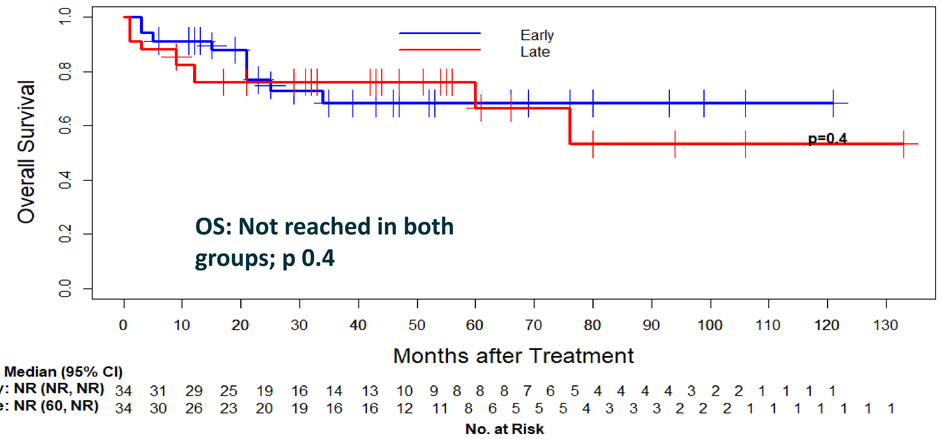
RESULTS

- Among 153 patients (119 early, 34 late), propensity score matching identified 34 matched pairs.
- No significant differences were observed in overall survival or progression-free survival between early and late treatment groups. Overall immune-related adverse event rates were comparable.
- Findings remained consistent in analyses restricted to first-line immunotherapy and advanced unresectable/metastatic melanoma.

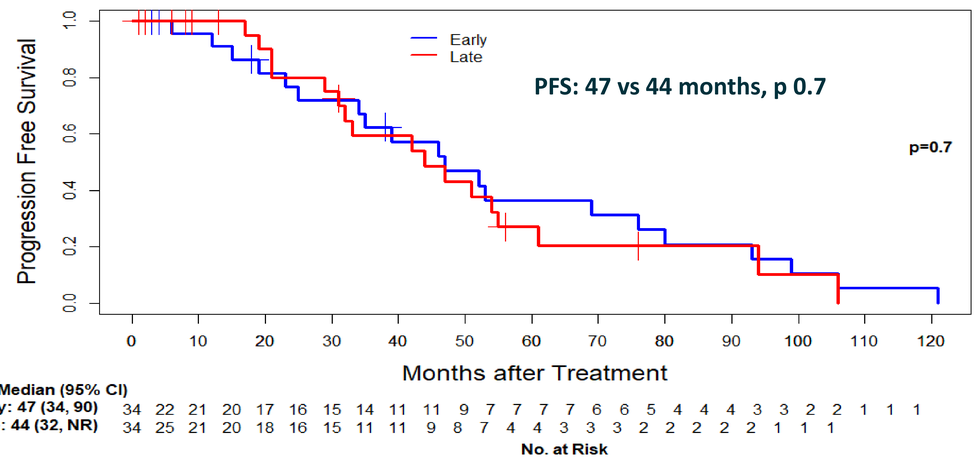
Endpoint	Early (n=119)	Late (n=34)	HR	95% CI	P value
Overall survival	Not reached	Not reached	1.51	0.57-3.97	0.4
Progression-free survival	47 months	44 months	1.13	0.59-2.20	0.7
Any irAE	22	19	-	-	0.61
Grade ≥3 irAE	14	5	-	-	0.017

Primary Outcomes: Overall Melanoma Cohort, propensity matched

Kaplan Meier Overall Survival



Kaplan Meier Progression Free Survival



AIMS

Primary Aim

- To evaluate whether early versus late induction immune checkpoint inhibitor administration is associated with overall survival in cutaneous melanoma.

Secondary Aims

- To compare progression-free survival and immune-related adverse events between early and late treatment groups.

CONCLUSIONS

- In this propensity score-matched real-world melanoma cohort, time of day of induction immune checkpoint inhibitor administration was not associated with significant differences in overall survival or progression-free survival.
- Findings were consistent across sensitivity analyses restricted to first-line therapy and advanced unresectable/metastatic melanoma.

CLINICAL IMPLICATIONS & FUTURE DIRECTIONS

- These findings do not support routine preferential scheduling of melanoma immunotherapy based solely on morning versus afternoon infusion time.
- Large multicenter studies are needed to determine whether chronotherapy effects exist in selected patient subsets or with specific immunotherapy regimens.
- Future analyses should evaluate infusion timing as a continuous variable and incorporate prospective circadian biomarker collection when feasible.

ACKNOWLEDGEMENTS

Research reported in this publication was supported in part by a grant from the J Walter Juckett Cancer Research Foundation and the University of Vermont Cancer Center. The content is solely the responsibility of the authors and does not necessarily represent the official view of the Foundation.

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