IMPACT OF CLONAL HEMATOPOIESIS ON CLINICAL OUTCOMES IN MELANOMA PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS

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Introduction

- **Clonal hematopoiesis (CH)** is an age-associated phenomenon which has been implicated in vascular diseases[1] and hematologic malignancies[2], and recent evidence suggests that CH may also influence responses to immunotherapy[3].

Aim

- To evaluate whether **CH status** impacts meaningful, patient-centered clinic outcomes among melanoma patients receiving immune checkpoint inhibitors (ICI).

Objectives

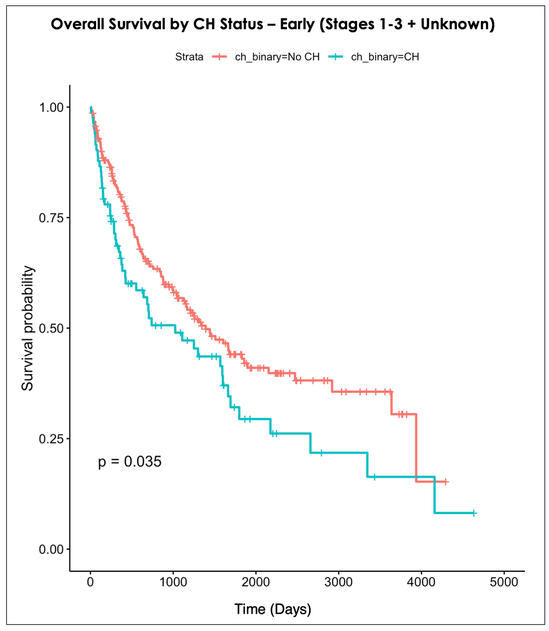
- Evaluate the impact of CH status on **progression-free survival (PFS)**, stratified by cancer stage.
- Evaluate the impact of CH Status on **overall survival (OS)**, stratified by cancer stage.
- Determine **CH prevalence** among melanoma patients compared to matched healthy controls.

Methods

- In a cohort of 361 melanoma patients who underwent pre-treatment blood-based genomic sequencing, CH was defined as somatic mutations in clonal hematopoiesis-associated genes with VAF > 2%.
- PFS and OS were measured from ICI initiation. Patients were stratified into early-stage (Stage I-III or unknown) and late-stage (Stage IV) cohorts.
- Survival analyses were assessed with Kaplan–Meier curves and log-rank tests; multivariable Cox proportional hazard models adjusted for age, sex, and baseline characteristics estimated hazard ratios (HRs) and 95% confidence intervals (CIs).
- Chi-squared analysis was conducted to assess CH prevalence among melanoma patients (n=361) when compared to a healthy control cohort (n=12,346) matched for age and sex, at an average 1:18 matching ratio.

Results

- **In the early-stage cohort, median OS was significantly shorter in the CH group** (2.8 vs. 3.8 years) by log-rank test (χ^2=4.4, p=0.04) and Cox regression (HR=1.43, p=.036).
- Early-stage CH-positive patients also demonstrated a non-significant trend towards shorter median PFS (6.6 vs. 9.9 months) by log-rank test (χ^2=2.2, p=0.10) and Cox regression (HR=1.25, p=0.14).
- In the late-stage cohort, CH-positive patients did not demonstrate significant differences in PFS (HR=1.01, p=0.96) or OS (HR=1.65, p=0.13).
- CH prevalence was significantly higher among cancer patients compared to matched healthy controls (27.7% vs. 21.4%; χ^2=7.94, p=0.004).



Summary

- Clonal hematopoiesis confers a significantly reduced overall survival among early-stage melanoma patients treated with ICI, as well as a trend towards shorter progression-free survival.
- CH prevalence was higher among melanoma patients compared to age and sex-matched healthy controls.
- Incorporation of CH profiling may enhance risk stratification and inform immunotherapy decision-making.

References

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3. Dogan, A., et al. (2021). *Clonal hematopoiesis is associated with adverse outcomes in immune checkpoint inhibitor-treated patients with non-small-cell lung cancer.*

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