Impact of β-Blockers on Outcomes following Dose-Adjusted EPOCH Chemotherapy in Aggressive Non-Hodgkin Lymphomas (NHL)

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Introduction

- **Peripheral nerves in the bone marrow** promote hematopoietic regeneration via **β2/3-adrenergic receptor signaling** in leptin receptor–expressing stromal cells.[1]
- In **allogeneic HSCT**, exposure to **non-selective β-blockers** has been linked to delayed engraftment and increased mortality.[2]
- The impact of **β-blockers on cyclical chemotherapy outcomes** remains unstudied.

Aim

To evaluate the impact of **selective** versus **non-selective β-blockers** on hematologic toxicity and survival in NHL patients receiving **dose-adjusted EPOCH chemotherapy.**

Objectives

- **Hematologic Toxicity**
  - Compare hematologic toxicity (median nadir and decline in Hb, platelets and absolute neutrophil count) between selective and non-selective β-blocker exposure during DA-EPOCH.
- **Survival**
  - Assess Progression-free (PFS) and Overall Survival (OS) differences by β-blocker exposure.
- **Chemotherapy Dose-Intensity**
  - Evaluate the impact of β-blocker use on chemotherapy dose-intensity.

Methods

- Retrospective analysis of 156 patients with aggressive NHL who received DA EPOCH +/- rituximab at UTSW between 2015-2024.
- **Exposure groups:**
  - β1-selective blocker
  - Non-selective β-blocker
  - No β-blocker
- **Endpoints:**
  - Hematologic toxicity
  - Dosing intensity of DA EPOCH
  - Dose modifications/delays
  - Incidence of Infections
  - Survival (OS, PFS).
- **Statistical analysis:**
  - ANOVA/t-tests for continuous variables
  - Fisher's exact/χ^2 for categorical variables
  - Kaplan–Meier with log-rank & Wilcoxon tests for survival analysis.

References

1. Nat Cell Biol. 2023 Dec;25(12):1746-1757.
2. Cancer Discov. 2025 Apr 2;15(4):748-766.

Results

- Of 156 patients, 22 received selective β-blockers, 13 non-selective β-blockers, and 121 received no β-blockers.
- **Hematologic Effects**
  - Hemoglobin and ANC decline: no significant differences between groups.
  - **Platelet count: significantly greater decline with β1-selective vs no β-blockers** (mean difference –66.3, p = 0.0093)
- No significant difference in infections or treatment delays between groups.
- **Survival**
  - **Overall survival differed across groups** (log-rank p = 0.0357).
  - **Significantly worse survival** in **selective β-blocker vs unexposed (p = 0.0103) [Fig 1].**
- **Dose Intensity**
  - **Selective β-blocker use: significantly reduced median and maximum DA-EPOCH dose-intensity compared to no β-blocker use (p <0.05) [Fig 2].**

Figure 1

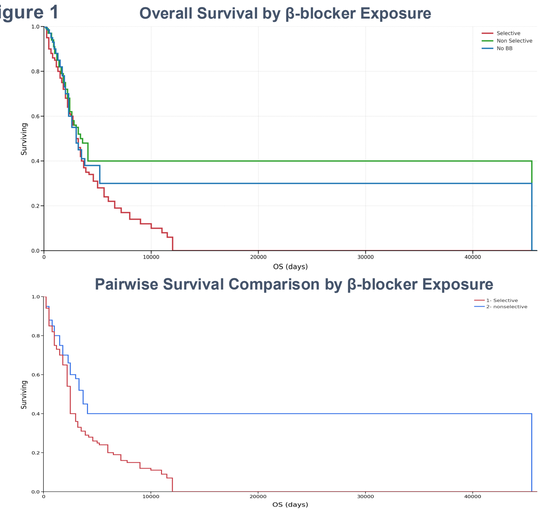
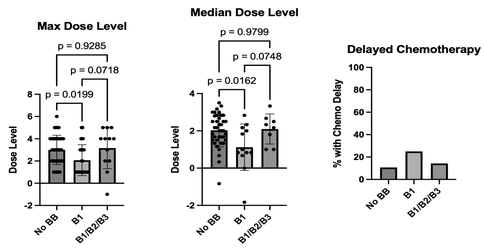


Figure 2 EPOCH Dose Intensity and Delay β-blocker Exposure



Summary

- **Selective β-blocker use:** greater thrombocytopenia, reduced dose intensity of DA EPOCH, and worse OS.
- **Non-selective β-blockers**: no significant effect on measured outcomes.

Discussion

- **Selective β-blocker use** was associated with **worse outcomes**, suggesting a **potential interaction between β1-adrenergic inhibition and cyclical chemotherapy-related hematologic or immune effects.**
- Prospective studies are needed to confirm this association and elucidate the mechanism.

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