CXCR4 EXPRESSION AS A DETERMINANT OF INFERIOR OUTCOMES FOLLOWING CD19 CAR T-CELL THERAPY IN DIFFUSE LARGE B-CELL LYMPHOMA: A NATIONAL CANCER DATABASE ANALYSIS

A. Owusu-Ansah[1], J. Ossai[1], Y. Reategui-Almonacid[1], J. Patel[1], V. Osei-Bonsu[1], A. Cohen[1]

1. Rutgers Newark Beth Isreal Medical Center , Newark NJ

RWJBarnabas HEALTH | Newark Beth Israel Medical Center

INTRODUCTION

- Diffuse large B-cell lymphoma (DLBCL) remains the **most common aggressive non-Hodgkin lymphoma**. CD19-directed CAR T-cell therapy has substantially **improved outcomes** in relapsed/refractory disease.
- Durable responses remain limited to approximately **40–50%** of patients.
- Elevated **CXCR4 expression** has been associated with **poor prognosis** across several B-cell malignancies, yet its effect on CAR T-cell efficacy remains incompletely understood.

AIM

To determine whether elevated CXCR4 expression is associated with inferior clinical outcomes following CD19 CAR T-cell therapy in patients with relapsed/refractory DLBCL

METHOD

STUDY DESIGN
Retrospective cohort study using the **National Cancer Database**, covering **2018–2023.**

POPULATION
Adults with **DLBCL** receiving **CD19-directed CAR T-cell** therapy.

TOTAL COHORT
1,842 patients included in the analysis.

PATIENTS STRATIFIED ACCORDING TO:

- High CXCR4 expression
- Low CXCR4 expression

USING:

- Immunohistochemistry (IHC)
- RNA-sequencing surrogate expression

KEY ENDPOINTS

- Overall Response Rate (ORR)
- Progression-Free Survival (PFS)
- Relapse Rate

RESULTS

Overall Response Rate

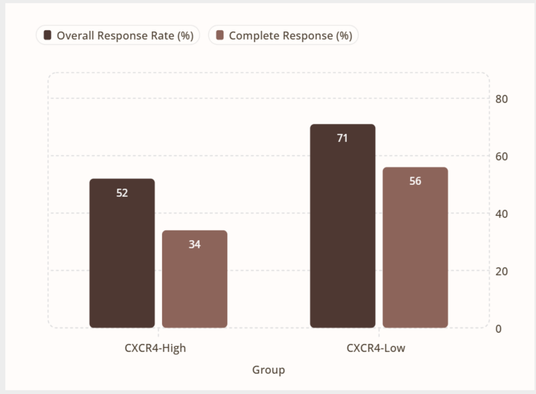

Figure 1. CXCR4-high patients had significantly lower ORR (52% vs 71%, p<0.001) and inferior complete response rates (34% vs 56%).

Progression-Free Survival

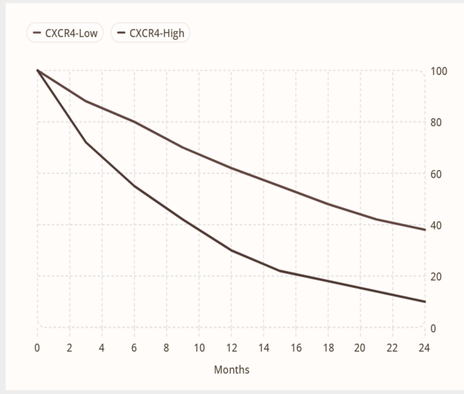

Figure 2. CXCR4-high expression demonstrated significantly shorter median PFS compared with CXCR4-low patients (6.8 vs 14.2 months; HR 1.78, 95% CI 1.52–2.09; p<0.001).

Relapse & Multivariable Analysis

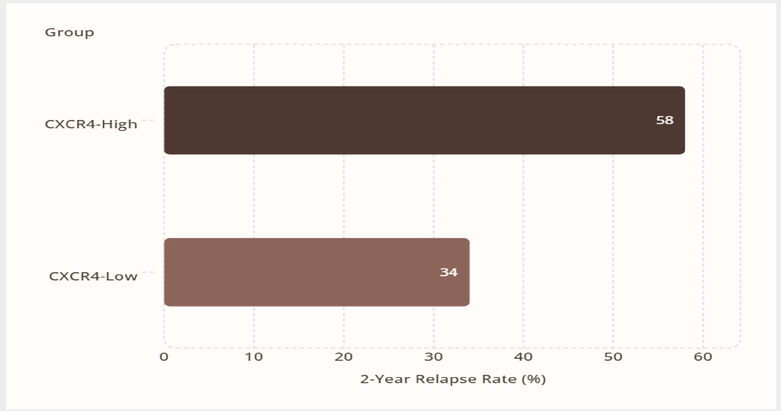

Figure 3. 2-Year Relapse: Significantly higher in the CXCR4-high cohort (58% vs 34%; p<0.001). Multivariable Analysis: CXCR4-high expression remained independently associated with shorter PFS (adjusted HR 1.61; p<0.001) and lower odds of response (adjusted OR 0.48; p<0.001).

CONCLUSIONS

- **High CXCR4 expression** is independently associated with **inferior outcomes** following CD19 CAR T-cell therapy in relapsed/refractory DLBCL.
- Patients with elevated CXCR4 experienced significantly **lower response rates, shorter progression-free survival,** and **higher relapse rates.**
- The findings support the CXCR4–CXCL12 axis as a **clinically relevant mechanism of CAR T resistance.**
- Combining CAR T-cell therapy with CXCR4-directed agents represents a **promising therapeutic strategy** that warrants **prospective clinical evaluation.**

FUTURE DIRECTIONS

- **Prospective** multicenter validation of CXCR4 as a predictive biomarker for CAR T-cell outcomes.
- Development of **multimodal risk models** integrating CXCR4, ctDNA, and clinical risk factors for personalized treatment selection.
- Investigation of **dynamic CXCR4 expression** as a biomarker for early relapse and treatment resistance.

CONTACT INFORMATION

Albert Owusu-Ansah, DO

Email: Aowusuansah95@gmail.com

Rutgers Newark Beth Israel Medical Center, Newark, NJ