# Developing a Pediatric CAR T-cell Comorbidity Index: Evaluation of Pre-existing Models in Pediatric B-ALL Patients

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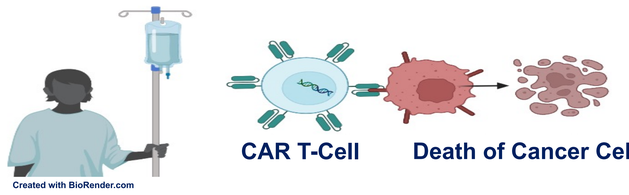
## Introduction

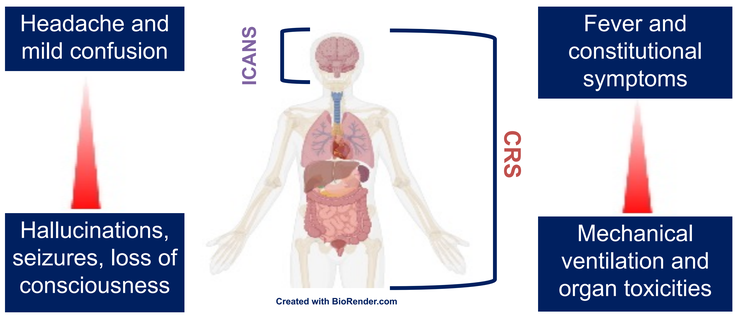
- **B-cell acute lymphoblastic leukemia (B-ALL)** is a hematologic malignancy of B-lymphocytes and is the most common cancer of childhood
- **Chimeric antigen receptor (CAR) T-cell** has shown remarkable efficacy particularly in those with **relapsed/refractory B-ALL.**

CAR T-Cell Therapy Mechanism of Action




- Genetic modification of **patient's own T-cells** allows MHC-independent recognition of the target antigen

CAR T-Cell Therapy Toxicities




- Despite promising efficacy, CAR-T cell therapy is associated with significant side effects; the two most notable toxicities are **cytokine release syndrome (CRS) and immune effector cell- associated neurotoxicity syndrome (ICANS)**.
- Occurrence and severity of post-treatment toxicities and outcomes vary among individuals → **A predictive model may help prognosticate each patient's risks of toxicities and outcomes.**
- **Importance of predictive models** in predicting post CAR T-cell therapy toxicities and outcomes
  1. Risk assessment and treatment decision making
  2. Patient counseling and education

## Aims

1. Test **existing adult-validated predictive models of CAR associated toxicities** in pediatric patients with B-ALL including the M-EASIX and CAR-HEMATOTOX model.
2. To determine if the **M-EASIX** and **CAR-HEMATOTOX** model can predict post-CAR outcomes including:
   - **CRS** and **CRS Maximum Grade**
   - **ICANS** and **ICANS Maximum Grade**

## Methods

1) Literature review of validated predicted models

- **m-EASIX Model** – Adapted from the EASIX model, a marker of endothelial damage that correlates with outcomes in allogenic hematopoietic cell transplantation.

| Predictors | Time Collected | Outcomes |
|---|---|---|
| • [LDH x **CRP**]/Platelets | • Start of lymphodepletion, Day -1, Day +1, Day +3, Onset of CRS | • Development of Severe CRS (≥3) and Severe ICANS (≥3) |

- **CAR-HEMATOTOX Model**: The CAR-HEMATOTOX model provides a tool for healthcare professionals to assess the risk of hematologic toxicities in patients undergoing CAR T-cell therapy for relapsed/refractory large B-cell lymphoma.

| Predictors | Time Collected | Outcomes |
|---|---|---|
| • Absolute neutrophil count, Hemoglobin, platelets, C-reactive protein, and Ferritin | • Before lymphodepletion within three days | • Severe neutropenia for greater/equal to 14 days between days 0 and 60 |

2) Test validated models in **pediatric patients with B-ALL**

3) Demonstrate predictive power or create new model

## Progress

- Data collection completed for 112 of patients with B-ALL treated on three trials**.**
- Initiated collaboration with bioinformatics to evaluate the **predictive accuracy, reliability, and generalizability** of the M-EASIX and CAR HEMATOTOX model to provide valuable insight for clinical decision-making

## Future Directions

- Develop and validate a comprehensive CAR Comorbidity index specifically designed for pediatric patients with B-ALL undergoing CAR T-cell therapy.
- Index will incorporate components of existing models currently undergoing testing with additional **comorbidities, biomarkers, disease-based risk factors** to accurately predict potential toxicities and outcomes

## Conclusions

CAR T-cell therapy offers hope for patients with limited options and demonstrates the potential for targeted and personalized approaches to cancer treatments.

Evaluating existing predictive models will benefit and optimize treatment approach to improve outcomes of CAR T-cell therapy in pediatric patients with B-ALL.

A pediatric specific CAR comorbidity index will allow patients and providers understand the expectations of toxicity which will improve patient care and enhance therapy effectiveness.

## References

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4. Figures created with BioRender.com

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