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Adios Adjuvant: Combination Immunotherapy for Pediatric Acute Lymphoblastic Leukemia (ALL) Patients

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ADIOS ADJUVANT

COMBINATION IMMUNOTHERAPY FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) PATIENTS

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INTRODUCTION

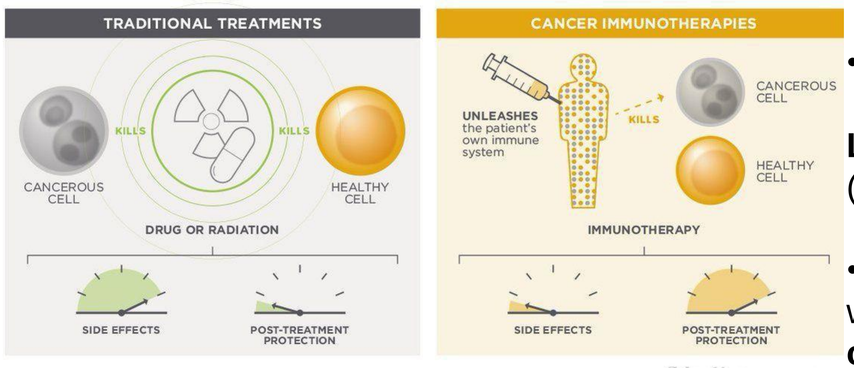


Figure 1. Immunotherapies has less side effects and prolonged protection from chemotherapies (ACS, 2020).

- Around 60% of pediatric cancers cases are **Acute Lymphoblastic Leukemia** (Lee, et al. 2016).
- Chemotherapy was once believed to be a **cure** for multiple cancers (ACS, 2020).
- Chemotherapy has **intense side effects** with **less prolonged protection** compared to immunotherapies (**Figure 1**).
- Am immunological approach to the treatment of cancer is **less traumatic** to the body and yields **higher remission rates** than previous adjuvant therapies.
- Common immunotherapies include **monoclonal antibodies** (A), **checkpoint blockade inhibitors** (B), and **CAR T cell therapy** (C) (Frey, 2019).

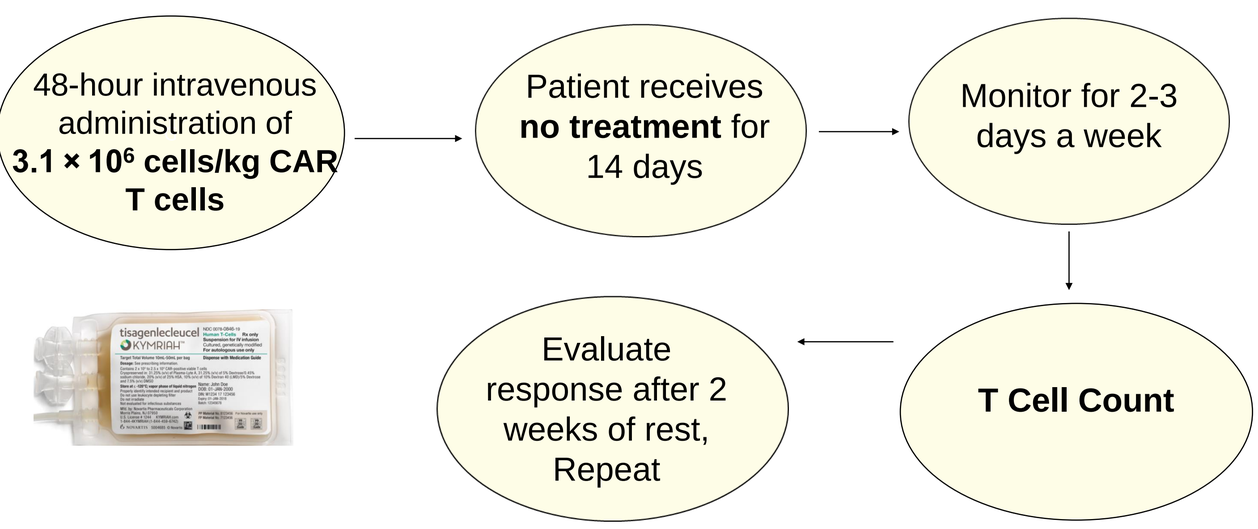
HYPOTHESIS

If two successful independent immunotherapies, **Kymriah® and Blinatumomab**, are combined and administered via repeated intravenous injections, then patients with Acute Lymphoblastic Leukemia will **achieve higher rates of remission** than if only one immunotherapy was administered.

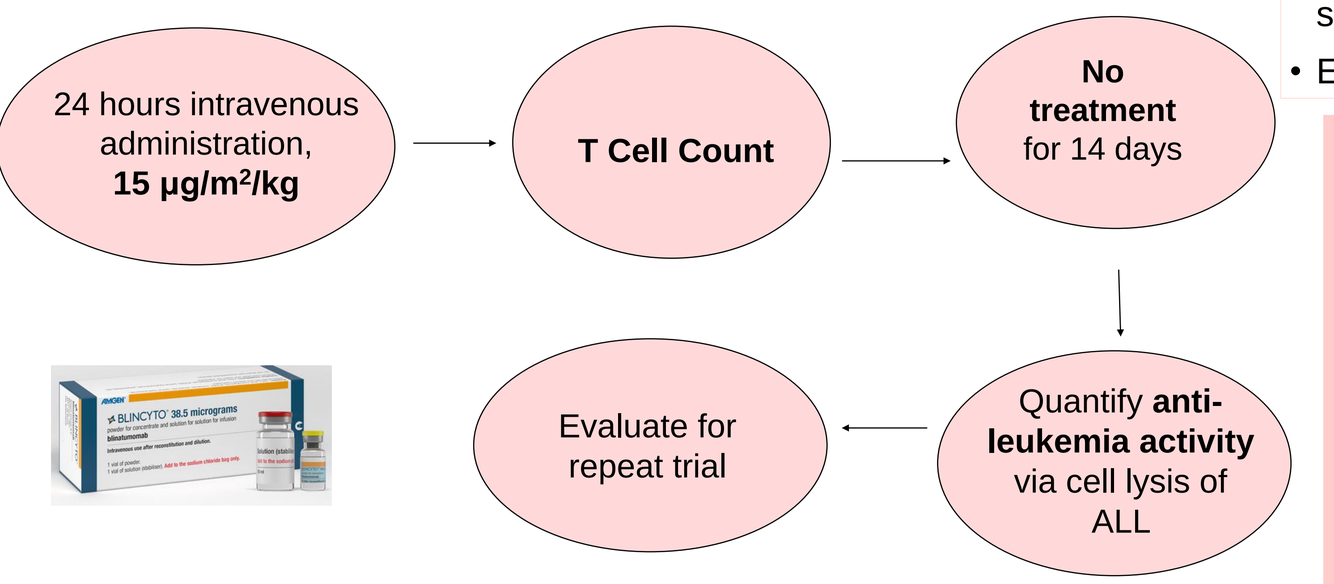
PROPOSED METHODS

- Test Group of 30 children with **relapsed ALL** will recieve simultaneous injections of Kymriah and Blinatumomab

Kymriah®



Blinatumomab



EXPECTED RESULTS

- **Kymriah®**
  - **75% Remission Rate for** all patients
  - **19 months** until remission is reached
  - **50%** of patients will have **event-free survival**
  - In remission **for 61 months** before more treatment is needed (average).

Table 1

Supporting data for FDA approval of tisagenlecleucel for r/r B-ALL (≤ 25 years)

Drug	Tisagenlecleucel
Indication	r/r B-ALL (≤ 25 years)
Clinical Trial	ELIANA (NCT02228096)
Overall Survival (N)	75
12-month OS (%)	76
95% CI	(63–86)
Median OS (mos)	19.1
95% CI	(15.2 – NE)
Event-free Survival (N)	73
12-month EFS (%)	50
95% CI	(35–64)
Duration of Remission (N)	61
Median (mos)	NR

Table 1. The responses in a test group of 38 pediatric leukemia patients in secondary relapse after steady dosage of Kymriah for 48 hours and 14 days of no treatment (Boyiadzis, 2018).

- **Blinatumomab**
  - **Over 50%** will achieve complete remission
  - Only **4% incidence of CRS** (Cytokine Release Syndrome)
  - **14%** of test group achieved **MRD** (Minimum Disease Response)

Table 1

Clinical trials of blinatumomab and outcomes

Clinical trial	Phase of trial	Population	Dosing	Primary end points	Secondary end points	Number of patients
Von Stackelberg et al, 201620	Phase I/II	Median age: 8 years; relapsed or refractory B-cell ALL	Phase I: maximum tolerated dose of blinatumomab was 15 µg/m²/24 hours, initiated at 5 µg/m²/24 hours for	Phase I: MTD; Phase II: CR rate within the first two cycles 32%	Phase II: proportion of patients HSCT post-Tx among responders 48%: RFS	Phase I: 49; Phase II: 44

Table 2. Responses of a test group of 44-49 patients to a maximum dose of 15 µg/m2/kg Blinatumomab. Responses differed based on trial phase and relapse phase.

IMPLICATIONS

- Combining two successful immunotherapies is likely to result in a **high success rate** (near 100%).
- In most studies, side effects of immunotherapies were **incomparable** to **adjuvant therapies** (1-4% incidence).
- **Cost of T cell therapies** is a major complication of the availability of this research ($800K-$1M).
- **Cytokine release syndrome** is a constant battle for immunotherapies that is being heavily researched in clinical trials.
- The **quality of life** of pediatric patients will be significantly improved during treatment.

PROJECT AIM

The goal of the experiment is to take two successful treatments for ALL with minimum 50% remission rates, **Blinatumomab and Kymriah**, and combine them to create a non-invasive, FDA approved immunotherapy with a near 100% remission rate within 10 years.

FUTURE STUDIES

- Begin **in vitro studies** to test for CRS and side effects of combination of therapies
- Progress to **in vivo studies** in mice to test how drugs interact in circulatory system of model organism with ALL
- Eventually progress to a series of **clinical trials** to get FDA approval

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