Preventing Relapse After Bone Marrow Transplant in Pediatric Acute Lymphoblastic Leukemia with a Personalized Treatment

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SUMMARY STATEMENT

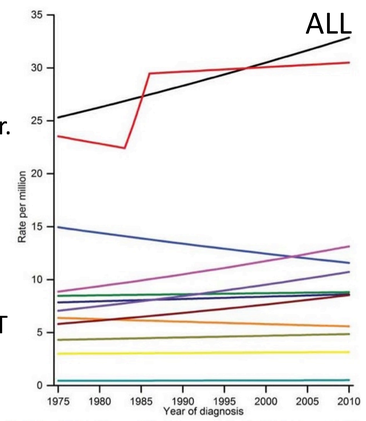
Feasibility and safety of identifying children with acute lymphoblastic leukemia (ALL) who are at risk of relapse after bone marrow transplant and treating with daratumumab, blinatumomab or traditional immune modulation to prevent relapse

DISEASE/CONDITION

ALL affects approximately 3,000 children per year in the US, and its incidence is increasing. Additionally, relapsed pediatric ALL, while rare, is the 6th most common pediatric cancer.

Most ALL relapses are treated with hematopoietic stem cell transplantation (HSCT).

Further relapses that occur after HSCT have extremely poor survival, with only 10-35% of children surviving long-term.



CURRENT TREATMENT

Current treatments for relapsed ALL are highly intensive, requiring long stays in the hospital and with high risks of treatment-related toxicities.

Most children who relapse with ALL undergo HSCT, one of the most intensive therapies we use for children. Even with HSCT, children with ALL may still relapse again.

New approaches to prevent ALL relapse are urgently needed.

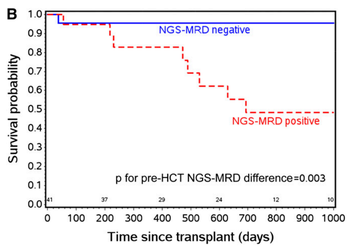
Problem: we can't tell who is going to relapse with current approaches.

PROPOSED TREATMENT

Repurposing next generation sequencing and FDA-approved drugs early after HSCT to prevent disease recurrence in patients with a high risk of relapse.

We hypothesize that prevention of ALL relapse after HSCT is possible with early detection and intervention. Our goal is to optimize early detection by repurposing state-of-the-art diagnostics to direct patients to targeted and personalized treatment interventions before relapse occurs. We will also repurpose immunotherapies in this novel setting to prevent relapse after HSCT.

Highly sensitive tests called "next generation sequencing (NGS)" can detect extremely low levels of leukemia cells called "measurable residual disease (MRD)". Patients with detectable MRD before transplant have worse outcomes. We will use NGS MRD after HSCT to find those patients with the highest chances of relapse and match them to personalized immune treatments based on the cellular features of their individual leukemia.



The drugs utilized in the immune treatments will include:

- Daratumumab: currently used to treat adult cancer called multiple myeloma and very effective at killing pediatric ALL cells in mice
- Blinatumomab: currently used to treat relapsed ALL, which will be repurposed to prevent relapses after HSCT

PROJECT

Prevention of Relapse by Employing Early MRD-directed therapy in Post-Transplant Acute Lymphoblastic Leukemia (PREEMPT ALL): a pilot phase 1 feasibility study to establish that NGS MRD can be used post-HSCT to deliver personalized therapy to prevent pediatric ALL relapse.

We will enroll 10 participants each onto three treatment strata based on the patient's ALL features:

- Stratum 1: CD38-positive ALL → daratumumab
- Stratum 2: CD19 positive ALL → blinatumomab
- Stratum 3: CD38/CD19-negative → reduction of immunosuppression ± donor lymphocyte infusion

If this new and innovative approach to relapse prevention is effective, it could provide patients and families with reassurance of more accurate prediction of ALL relapse risk, as well as novel, safe, and effective treatment options. This approach also could be applied to other hematologic malignancies, such as multiple myeloma, chronic lymphocytic leukemia, and acute myeloid leukemia.


Photo Courtesy of The Children's Hospital of Philadelphia

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