

# CATCHAML Q & A

## with the Principal Investigators

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**PAULINA VELASQUEZ, MD,**  
Co-Principal Investigator



**SWATI NAIK, MBBS,**  
Co-Principal Investigator

### **Why is this study being done?**

Approximately 30% of children with AML relapse and less than 40% of those who relapse are ultimately cured. Increased toxicities have dampened the effect of intensive chemotherapy regimens and hematopoietic cell transplant (HCT) on overall survival. This highlights a need for novel and targeted therapeutic options.

CATCHAML will be the first AML-directed CAR T-cell clinical protocol at St. Jude Children's Research Hospital. We serve a relapsed/refractory CD123+ AML patient population that needs new cancer-directed therapies. St. Jude has extensive clinical experience with high-risk AML patients and their associated complications. Although there are other institutions evaluating AML-specific CAR T-cell therapy, the safest and most effective construct remains to be determined. In addition, the dosing schedule and the best management strategy for possible side effects are still unknown.

### **How does this treatment target the disease?**

As opposed to the treatment of B-ALL targeting CD19, targeting AML has proven challenging given that the majority of the targeted antigens are also expressed at low levels on normal hematopoietic cells. CD123 is an AML-associated antigen that is expressed on leukemic blasts and is enriched in the cancer stem cell population. Preclinical data generated by our group and other investigators have shown promising results in AML treatment with engineered immune effectors directed to the CD123 antigen.

## **What makes this different from the other CAR T-Cell protocols for AML?**

Early phase clinical studies using CD123-CAR T cells in an adult-focused population are in progress (NCT02159495, NCT03190278). Our trial is geared to pediatric and young adult patients with relapsed/refractory, CD123+ AML. In addition, our vector expresses CD123-CAR as well as a CD20 molecule. The latter functions as a safety switch and allows for selective depletion of the genetically modified cells. We produce this vector using a transient producer cell line on the St. Jude campus at the Good Manufacturing Practices (GMP) facility.

## **What is the rationale for this specific lymphodepletion regimen?**

Lymphodepletion has been shown to be critical for the anti-tumor efficacy of adoptive cell therapies. The most commonly used lymphodepleting regimens combine cyclophosphamide and fludarabine (Cy/Flu), which have contributed to the dramatic clinical responses seen with CD19-CAR T cells for ALL, including our FDA-approved CD19-CAR T cell therapy study (SJCAR19). We therefore chose a Cy/Flu regimen for this study.

## **How were the eligibility criteria developed?**

The relapsed and refractory disease inclusion criteria for CATCHAML are modeled after the disease classification criteria that is currently being used by the St. Jude Leukemia Division. They are intended to provide those patients with relapsed or refractory disease, a novel therapeutic option that serves as a bridge to HCT. Patients therefore need to have an identified suitable HCT donor. Additionally, CATCHAML will provide a treatment option for those patients that relapse after HCT or experience multiple relapses, a patient population that is historically difficult to treat using conventional therapy.

There are two parts to the eligibility criteria: one for procurement and manufacturing of CD123-CAR T cells, and a second one to proceed with treatment with CD123-CAR T cells. If available, a previously frozen, autologous leukapheresis product can be used for T-cell production. When CD123-CAR T cells have been successfully manufactured for an individual patient and the patient meets eligibility criteria to receive therapy on this protocol, they will be consented to proceed with the treatment portion of the study.

## **How long will patients be monitored after completion of therapy?**

Long-term follow-up will occur for 15 years after product infusion. Patients will continue to be monitored on our protocol for the first year post CD123-CAR T-cell infusion and will then transition to our existing institutional protocol for long-term follow-up of patients who have received gene therapy or gene marked products (GENEFU).

**For more  
information,  
contact:**

### **Physician/Patient Referral Office:**

referralinfo@stjude.org

901-595-4055

1-888-226-4343 (toll-free)