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Haploidentical IL-15/41BBL activated and expanded natural killer cell infusion therapy after salvage chemotherapy in children with relapsed and refractory leukemia

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ABSTRACT

Primary refractory or relapsed pediatric leukemia yield significant morbidity and

mortality, with long-term survival rates < 40%. Here we present a post-hoc analysis

assessing safety and efficacy of infusing activated and expanded Natural Killer cells

(NKAE) from haploidentical donors in patients from 2 clinical trials. In total, 18

children, adolescents and young adults with relapse or refractory acute leukemia were

treated with two cycles of rescue chemotherapy followed by fresh NKAE cells infusions

and low doses of IL-2. The overall response rate, complete remission achievement at the

end of the study, was 72% (13 of 18). We infused 52 NKAE cell products containing a

median of $6.76x10^6$ NK cells/kg (0.7-34.16) and $0.49x10^6$ T cells/kg (0-11). All

infusions were well tolerated with no graft versus host disease nor other serious adverse

events. Among the 14 patients who completed treatment, 4 of them are alive and

leukemia-free more than 750 days post-transplant. We conclude that infusion of fresh

NKAE cell therapy is feasible and safe in heavily pretreated pediatric population, and

should be further investigated in advanced-phase clinical trials as well as a

consolidation therapy to decrease relapse in patients with high-risk leukemia.

Running title: Activated NK cell therapy in pediatric refractory leukemia

Key words: Natural killer cells, Hematopoietic stem cell transplantation,

Immunotherapy, Acute myeloid leukemia, Lymphoblastic leukemia, Myeloblastic

leukemia

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