

POSTER PRESENTATION

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Transient regulatory T-cell (Treg) depletion with IL-2 diphtheria toxin fusion protein enhances clearance of acute myeloid leukemia by haploidentical natural killer (NK) cells

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Adoptive transfer of haploidentical natural killer (NK) cells can induce remissions in patients with AML. Despite lymphodepleting chemotherapy failure may result from suppression by host regulatory T cells (Treg). We report outcomes of 57 refractory AML patients treated with cyclophosphamide and fludarabine followed by haploidentical NK cells and exogenous IL-2 to facilitate NK proliferation. We augmented Treg lymphodepletion with IL-2-Diphtheria toxin fusion protein (IL2DT) in 15 subjects. NK cell-enriched product characteristics are described for three production methods. Day 14 blood donor NK expansion rates were 10% (no IL2DT) versus 30% (with IL2DT) and day 28 leukemia clearance were 25% versus 53% (with IL2DT; $p=0.06$), suggesting clinical efficacy of IL2DT strategy. Host Treg depletion at day 7 after IL2DT (mean 1% [range 0-4.7%]) correlated with donor NK cell expansion ($p=0.01$). The only factor correlating with AML clearance was donor chimerism detectable a week after NK cell infusion (mean 49.5%). In vitro, Tregs co-incubated with NK cells exhausted added IL-2 (0.25ng/ml) and suppressed NK cells proliferation. Higher amounts of IL-2 (10ng/ml) or IL15 (0.5ng/ml) lead to unaltered NK cell proliferation in vitro even at high NK:Tregs ratios. Future clinical improvements in adoptive cell therapy might include alternate methods of Treg depletion and the use of IL-15 to augment NK cell expansion.

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