

## Autologous Umbilical Cord Blood Transfusion in Very Young Children with T1D: 1 Year Follow-Up

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Interest continues to grow regarding the potential of umbilical cord blood (UCB) therapies to modulate autoimmune disease. We conducted an open label, phase I study utilizing autologous UCB infusion to ameliorate established type 1 diabetes (T1D). Twenty-three patients underwent a single intravenous infusion of autologous UCB cells (NCT00305344; FDA IND BB-11918). Intensive insulin regimens were employed to optimize glycemic control. Metabolic and immunologic assessments were performed before infusion and 3, 6, 9, 12, 18, and 24 months post-infusion. Of the 23 patients, 15 have completed 1 year of post infusion follow up. Of the 15, mean age at infusion was  $5.7 \pm 2.6$  yr, with mean post-diagnosis time at infusion  $0.5 \pm 0.6$  yr. Pre-infusion median (interquartile range) metabolic values were: HbA1c 7.0% (6.1-8.3), insulin use 0.42 units/kg/d (0.21-0.55), and peak c-peptide 0.93ng/mL (0.7-2.03). A median of  $1.50 \times 10^7$  total nucleated cells per kilogram with 96% viability were infused. No infusion related adverse events were observed. One year post infusion (average 18 months post diagnosis), median (interquartile range, P vs baseline) values were: HbA1c 7.0% (6.5-7.7,  $P=0.97$ ), insulin dose 0.67 units/kg/day (0.55-0.77,  $P=0.009$ ), peak C-peptide 0.50 ng/mL (0.26-1.30,  $P=0.002$ ). The fractional change in peak C-peptide was -52.3% ( $P=0.002$ ). In comparison, median HbA1c and insulin use 18 months post-diagnosis in a historical control group of 30 age-matched children (mean age 5.28 yr at diagnosis) were 7.6% and 0.73 units/kg/d, respectively. Patients receiving UCB infusion had increased levels of peripheral blood regulatory T cells 6 months after infusion ( $P=0.06$ ). No changes were observed in CD4:CD8 ratio or in autoantibody titers.

Autologous UCB transfusion is safe and may slow rates of decline of endogenous insulin production in children with T1D. The observation of increased peripheral blood Treg following cord blood infusion mandates prolonged follow up and additional efforts to determine if specific cell populations derived from UCB elicit direct or indirect immunomodulatory effects and if UCB cells can be used as part of safe and effective therapies for T1D.

