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Clinical Trials – Regenerative Medicine

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Abstract 13

A Randomized, Placebo-Controlled, Phase II Trial of Intravenous Allogeneic Umbilical Cord Blood Infusion for Adults with Ischemic Stroke

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Introduction: Stroke is the fifth leading cause of death in the United States. Tissue plasminogen activator and mechanical thrombectomy are the only effective treatments, but many patients are ineligible for these treatments.

Objective: The objective of this study was to determine whether an intravenous infusion of a non-HLA matched, unrelated donor umbilical cord blood (UCB) would improve functional outcomes.

Methods: We conducted a phase II multicenter, randomized (2:1), placebo controlled, double-blinded trial of UCB in adults with acute ischemic stroke. Patients had to have adequate immune function. Cord blood units were selected from U.S. public cord banks based on blood type, race, and cell dose. Study product was infused 3-10 days post stroke. Participants were randomized within strata of National Institutes of Health Stroke Scale Score (NIHSS) (<12 vs ≥12), and study center. The primary endpoint was change in Modified Rankin Scale (mRS) (baseline minus day 90). The study was powered at 80% (odds ratio of 2). Key secondary outcomes included functional independence at day 90 (mRS <2), NIHSS, the Barthel Index, infusion reactions, and adverse events.

Results: Seventy-nine participants were enrolled at 6 centers when the trial was closed early due to slow accrual related to COVID19; 73 participants (47 randomized to UCB) were included in the safety and efficacy analyses. The median (range) of the change in mRS was 1 (–2, 3) in UCB and 1 (–1, 4) in placebo. A shift analysis based on the proportional odds model showed an odds ratio of 0.9 (95% CI: 0.4, 2.3) after adjustment for baseline mRS and randomization strata. No differences were observed on the key secondary outcomes. There were 17 mild infusion reactions (27.6% UCB; 15.4% placebo). The distribution of serious and non-serious adverse events was similar between arms.

Discussion: This study demonstrated the safety of infusing non-HLA matched UCB to adults with acute ischemic stroke. Feasibility and logistics were challenging. The primary efficacy endpoint did not demonstrate benefit in this underpowered sample size. In a secondary ad hoc analysis, a trend of improved functional outcomes at day 90 in recipients of UCB more than 5 days post stroke (Figure 1) could be explored in future trials.

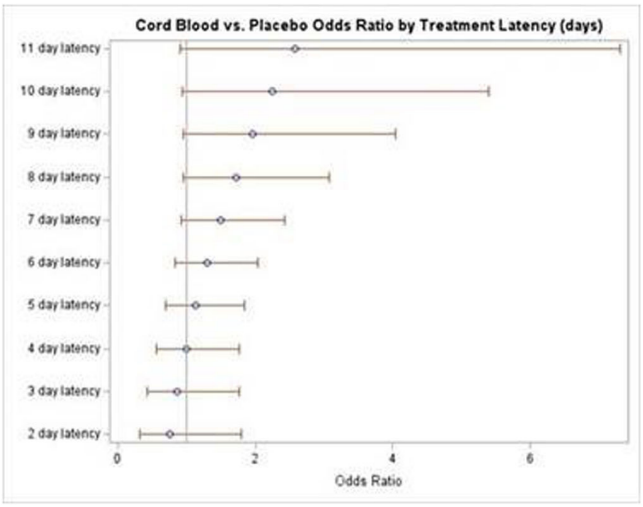

Figure 1. Cord blood versus placebo odds ratio by treatment latency (days).