

CYTOTHERAPY

The Journal of Cell Therapy

Cytherapy 2019; Volume 21, Issue 5, Supplement, Page S89-S90.

DOSE-DEPENDENT IMMUNOMODULATORY EFFECT OF INTRAVENOUS ALLOGENEIC UMBILICAL CORD-DERIVED MESENCHYMAL STROMAL CELLS (CYTOPEUTICS CLV-100) INFUSION IN HEALTHY VOLUNTEERS

SP Chin¹, KY Then², SK Cheong³

¹NSCMH Medical Centre, Seremban, Malaysia, ²Universiti Tunku Abdul Rahman University, Malaysia, ³Cytopeutics, Malaysia.

Background: Mesenchymal stromal cells (MSCs) express growth factors and other cytokines that stimulate repair and control the immune response. MSCs are also immunoprivileged with low risk of rejection. Umbilical cord derived MSC (UCMSCs) are particularly attractive as off-the-shelf allogeneic treatment in emergency medical conditions.

Objective: We aim to determine the safety and feasibility of intravenous allogeneic infusion of UCMSCs (CLV-100) by Cytopeutics (Selangor, Malaysia) in healthy volunteers, and to determine the effective dose at which an immunomodulatory effect is observed.

Methodology: Umbilical cord samples were collected after delivery of fullterm, healthy babies with written consent from both parents. All 3 generations (newborn, parents and grandparents) were screened for genetic mutations, infections, cancers and other inherited diseases. Samples were transferred to a certified Good Manufacturing Practice laboratory for processing. Subjects were infused with either low dose (LD, 65 million cells) or high dose (HD, 130 million cells) of CLV-100 followed up for 6 months. We measured cytokines level using ELISA including the acute phase reactant high-sensitivity C-reactive protein (hs-CRP), anti-inflammatory cytokines interleukin 1 receptor antigen (IL-1RA) and interleukin 10 (IL-10), and the pro-inflammatory cytokine Tumor Necrosis Factor-Alpha (TNF- α). The study was approved by the National Medical Research and Ethics Committee (MREC).

Results: 11 healthy subjects (LD, n=5; HD, n=6; mean age of 55±13 years) were recruited. All subjects tolerated the CLV-100 infusion well with no adverse reaction throughout the study. While there was no change in vital parameters and routine blood tests, there was a transient rise in hs-CRP at Day 3 post infusion (1.2±1.5 vs. 4.5±3.9 mg/L; p=0.03) which resolved at Day 7. The anti-inflammatory IL-1RA was significantly elevated in HD patients at 1 month post infusion (436±128 vs. 615±148 pg/mL; p=0.028). At 6 months, HD group had significantly higher levels of anti-inflammatory markers IL1-RA (705±160 vs. 306±36 pg/mL; p=0.02) and IL-10 (321±27 vs. 251±28 pg/mL; p=0.02); and lower levels of pro-inflammatory marker TNF- α (74±23 vs. 115±15 pg/mL; p=0.038) compared to LD group.

Conclusion: Allogeneic UCMSCs CLV-100 infusion is safe and well-tolerated in low and high doses. Anti-inflammatory effect is observed with high dose infusion.

