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Long-term Outcomes after Gene Therapy for Adenosine Deaminase-deficient Severe Combined Immune Deficiency (ADA-SCID)

Patients lacking functional adenosine deaminase activity suffer from severe combined immunodeficiency (ADA-SCID). A cohort of 10 ADA SCID patients, aged 3 months to 15 years, underwent gene therapy (GT) in a Phase II clinical trial between 2009-2012. Autologous CD34+ bone marrow cells were transduced with a gamma-retroviral vector (MND-ADA) and infused following low dose busulfan conditioning. Shaw et al. (2017) reported on the first two years of active evaluations in the gene therapy treatment trial, which has since been followed by a long-term follow-up protocol. All but one subject (15 years old at the time of GT and on chronic ERT since a few months after GT) remained without serious opportunistic infection or need to resume ERT or proceed to HSCT due to insufficient immune reconstitution. There was a broad range of responses, in terms of immune reconstitution, normalization of ADA enzyme and adenine metabolites in blood cells, that correlated with the variations in levels of engraftment of gene-corrected stem cells, as reflected in the vector copy number in granulocytes. These parameters were generally better in younger patients and those receiving higher doses of gene-marked CD34+ cells. Across subjects, median VCN in granulocytes correlated with CD19+ B cell count and absolute lymphocyte count (ALC). Three subjects remained off of immunoglobulin replacement therapy. No subject experienced a leukoproliferative event post GT. These long-term findings demonstrate enduring efficacy from gene therapy for ADA-SCID.