7. GENE THERAPY FOR ADENOSINE DEAMINASE SEVERE COMBINED IMMUNODEFICIENCY (ADA-SCID)

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Introduction. About 1 in 500,000 people are born with severe combined immunodeficiency (SCID). The adenosine deaminase variant is a fatal inborn error of purine metabolism. Accumulation of adenosine and deoxyadenosine leads to inhibition of DNA synthesis and repair, as well as abnormalities of thymocyte development, vital in an evolving immune system. Patients with ADA-SCID often die prematurely from infection. Currently, treatments include PEGylated enzyme therapy and allogenic stem cell transplantation from a matching HLA donor, however their success is variable. These treatments are also temporary, complicated, and carry a high risk of death. Gene therapy using a Lentiviral vector shows promising results for treatment of SCID.

Aim of study. Evaluating the current possibilities and post-treatment outcomes of implementing gene therapy for ADA-SCID.

Methods and materials. The study includes a specialized literature review of research/clinical trials published in PubMed, NIH, and the New England journal of medicine. Key words include “SCID” “Gene therapy”. Information contains results of studies done in Asia, Europe, and the United States evaluating efficacy, safety and long-standing outcomes of gene therapy for ADA-SCID with viral vectors.

Results. Comparing patients treated with PEGylated enzyme therapy and stem cell transplant, patients enrolled in clinical trials treated with Gene therapy (GT) demonstrated immune reconstitution, and event free survival. Treatment involves obtaining stem cells from the patient’s bone marrow. Once isolated the therapeutic genetic material is implemented into a lentiviral vector (LVV). The LVV can integrate the RNA into the nuclear DNA of the host target cells. The patients are given an injection of Busulfan to decrease their defective cells. The new cells are then transfused back to the patient, effectively coding for the deficient ADA gene leading to production of the enzyme. Results show decreased toxic metabolites and immune reconstitution. Although survival rates in patients treated with GT are 100%, clinical trials remain highly limited and commercial GT is not currently available.

Conclusion. Genetic therapy using Lentiviral vectors is an effective and safe treatment for patients with ADA-SCID. Long term outcomes show minimal complications and complete cure of the disease. The therapy remains limited due to resources and high costs.

Keywords. SCID, gene therapy, lentiviral vector.