T tolerance-induction with autologous tolerogenic dendritic cells treated with VITamin D3 and loaded with myelin peptides in Multiple Sclerosis (Tolervit-MS)

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Multiple sclerosis (MS) is an autoimmune disease of the central nervous system. Current treatments reduce disease activity but do not decrease long-term disability and have relevant side effects. Thus, there is an unmet need for safer and effective treatments. Autologous therapy with tolerogenic dendritic cells (tolDC) is a promising strategy for the attenuation of pathogenic T cells in autoimmune diseases. Our group has developed an antigen-specific cell therapy based on autologous vitamin D3 (VitD3)-tolDC loaded with myelin peptides.

In vitro studies have demonstrated a potent immunoregulatory activity of VitD3-tolDC reducing lymphocyte proliferation and IFN-γ production and increasing IL-10 levels, in co-culture experiments. Moreover, in vivo studies in the animal model of MS revealed a beneficial effect of VitD3-tolDC ameliorating the severity of the disease. Considering these pre-clinical results, as well as reported outcomes from previous clinical trials using DC, a clinical trial has just started recruitment.

Active MS patients will be included in a dose-escalation best-of-five design: Cohort 1 (5x10^6 VitD3-tolDC), Cohort 2 (10x10^6), Cohort 3 (15x10^6). A fourth Cohort of patients under IFN-beta treatment receiving the selected dose of VitD3-tolDC will be included. The trial protocol has been approved by the Spanish regulatory authorities (AEMPS) (Nº EudraCT: 2015-003541-26, available at ClinicalTrials.gov Identifier: NCT02903537, Tolervit-MS). Each cohort will received 6 administrations of tolDC (first 4 every 2 weeks and last 2 every 4 weeks). Clinical, MRI and immunological monitoring of 12 patients will be performed for 24 months. Each patient will be its own pre- and post-intervention control.

References: