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Results of a pilot clinical trial of DC-based vaccines for treatment of HCV-infection

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Antigen-specific CD4+ and CD8+T cells play a key role in pathogenesis and outcome of hepatitis C virus (HCV) infection. While the strong multiepitopic T cell responses predict successful viral elimination, a deficiency of adaptive immune response is associated with virus persistence. Dendritic cells (DCs) play a dominant role in T cell priming and maintenance of strong T cell response. The present paper contains results of an open pilot study of efficacy and safety of DC-based vaccines in the patients with chronic hepatitis C. Ten patients with genotype 1 HCV, viral load - RNA ≥10^4 IU/mL, without development to cirrhosis have been enrolled in this study. DCs were applied in 2 rounds of vaccination performed within 7 months. DCs were generated in presence of GM-CSF and IFNα and then loaded with recombinant viral proteins Core (1-120) and NS3 (1192 – 1457) genotype 1b HCV. T cell specific responses to viral antigens and mitogen reactivity to Concanavalin A were evaluated by H3 thymidine incorporation. Th1 and Th2 responses were measured by IFN- and IL-4 production by antigen-stimulated T cells. DC-based vaccines did not induce any serious side effects. Vaccination with Ag-loaded DCs resulted to an increase of proliferative response of mononuclear cells to viral antigens (mostly to Core), an induction of antigen-specific Th1 cells (with a peak response after the second course of vaccinations), restored initially low ConA-stimulated lymphocyte proliferative activity and did not lead to the generation of regulatory CD4+25+127-T cells. Though sustained reduction of viral load has not been achieved, the proliferative activity of mononuclear cells to viral antigens after the 1st course of vaccine negatively correlated with the viral load. The data obtained suggest that DC-based vaccines may be a promising approach to the enhancement of T cell specific immune response in patients with chronic hepatitis C.

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Indications, contraindications and outcomes in patients referred for liver transplantation

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Liver transplantation has become the standard treatment for end stage liver disease. Recent improvements have allowed successful transplantation of patients with primary liver cancer, hepatitis B and C, all forms of cholestatic liver disease, autoimmune hepatitis as well as fulminant liver failure. Selection of the right patients who are most likely to benefit from this life saving procedure is a complex task. In this presentation, I will discuss the indications and contraindications for liver transplantation as well as the evaluation process of patients to determine their liver transplant candidacy. With optimal selection, we can expect 1 year probability of survival of 90% and 5 year survival probability of 80%. This compares to less than 10% of 5 year survival in comparable patients who do not receive liver transplantation.

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