# 001011 | Immune impact of tolerogenic dendritic cells in patients with type 1 diabetes

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**Background:** Clinical trials of tolerogenic dendritic cells (tolDC) for treatment of type 1 diabetes (T1D) were performed (NCT05207995) with immunologic efficacy studied.

**Method:** Patients with newly diagnosed T1D (up to 12 months) who provided informed consent were included in the study. There were 16 patients in the study group (R) treated with tolDC and 17 patients in the control group (C) not treated with cellular therapy. Serum samples ($n=33$) were analyzed for autoantibodies (AA) to key pancreatic islet antigens: glutamic acid decarboxylase 65 (GAD65), insulinoma-associated protein 2 (IA-2), zinc transporter-8 (ZnT8), and islet cell cytoplasmic antigens (ICA) using ELISA. Whole blood ($n=16$) was incubated for 6 h with a pool of peptides, covering sequences of GAD65, IA-2 or insulin. Counts (%) of $CD3^+IFN\text{-}g^+$ antigen specific T cells ASCs were further assayed by flow cytometry.

**Results:** Before cell therapy 88.0% of patients in the R group and 82.4% in the C group were positive to GAD65 ($p>0.05$); 37.5% of R and 35.3% of C patients had IA-2 ($p>0.05$); 62.5% of R and 70.6% of C patients had Zn8 AA ($p>0.05$). All T1D patients were negative to ICA AA. After cell therapy a decrease in the levels of GAD and IA-2 AA in the R group was detected (GAD-65 before – 88.0%, after 62.5%, $p<0.05$; IA-2 before – 37.5%, after 12.5%, $p<0.05$). In the C group, changes in the level of AA were not observed ($p>0.05$). Before cell therapy in the R group only 1 of 16 patients (6.25%) were positive for GAD65-reactive ASCs and 1 of 16 patients (6.25%) was positive for insulin-reactive ASCs. IA-2 ASCs were not detected. After cell therapy ASCs 1 of 16 patients (6.25%) was positive for GAD65-reactive ASCs, 2 of 16 patients (12.5%) were positive for IA-2-reactive ASCs, 1 of 16 patients (6.25%) was positive for insulin-reactive ASCs, and 1 of 16 patients (6.25%) was positive for GAD65 and IA-2-reactive ASCs. 1 patient, whose blood sample before cell therapy was positive for insulin-reactive ASCs, also had these ASCs after cell therapy.

**Conclusion:** After cell therapy with tolDC, the levels of AA to the B-cell components GAD65 and IA-2 decreased in the T1D patients. In 70% of patients, treatment with tolDC gave no increases of ASCs as well as no expansion of the spectrum of autoantigens involved in autoimmune T-cell reactions, suggesting treatment with tolerogenic dendritic cells led to absence of progression of the autoimmune processes.

**Conflicts of Interest:** The authors did not specify any links of interest.

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