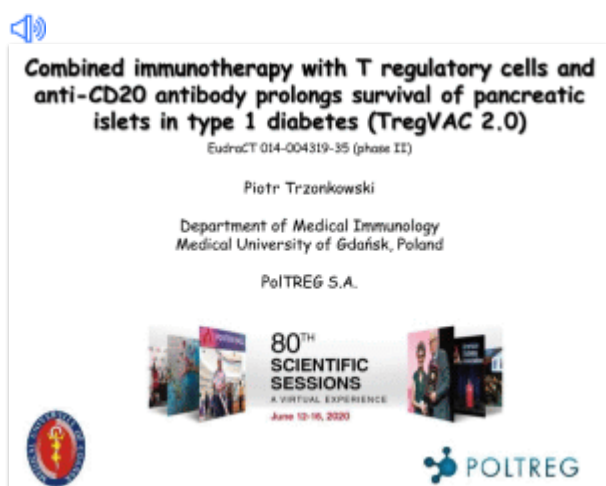


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ADA

Combined Immunotherapy with T Regulatory Cells and Anti-CD20 Antibody Prolongs Survival of Pancreatic Islets in Type 1 Diabetes



Clinical Therapeutics/New Technology - Diabetes Prevention

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Ask the Author

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Background: Immunotherapy using T regulatory cells (Tregs, Tr) prolongs remission in type 1 diabetes (T1DM) but the effect fades with the time. Here, we report phase II trial in which Tregs therapy was combined with anti-CD20 antibody (TrCD20) to make the effect more sustained.

Methods: Thirty-six children with newly diagnosed T1DM were randomized 1:1:1 into the following groups: Tr, TrCD20 and control. The treatment in Tr group consisted of autologous expanded CD3⁺CD4⁺CD25^{high}CD127⁻ Tregs in the two doses (30x10⁶ of Tregs/kg b.w. each), three months apart. TrCD20 group received additionally 4 doses of rituximab (375 mg/m², each) between the first and second dose of Tregs. Control group was left without the treatment and all patients were followed for 2 years.

Results: The best results were found in TrCD20 group, who was characterized by stable serum levels of both fasting C-peptide and stimulated C-peptide in glucagon and MMT tests throughout the entire trial (for fasting C-peptide only 20% decrease at +24months when compared to baseline). Tr group was characterized by stable levels of fasting and stimulated C-peptide up to +12months and then it dropped gradually until the end of the trial. As compared to control group, there was a better glycemic control measured as HbA1c and mean fasting glucose in both interventional groups throughout the whole follow up. TrCD20 group was in partial remission defined as insulin dose below 0.5IU/kg up to +21 months. The longest insulin independent follow up lasted 18months. The end of the remission in Tr group was noted at +18month and in controls at +12months. At the +24months daily insulin requirement and HbA1c levels were significantly lower in TrCD20 as compared to control group.

Conclusions: The combined immunotherapy with Tregs and anti-CD20 antibody prolonged the most significantly survival of pancreatic islets in T1DM children. Trial registration: EudraCT: 2014-004319-35.

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