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TNF-? inhibitors for type 1 diabetes: exploring the path to a pivotal clinical trial

Cassandra Bazile, Margy M. Abdel Malik, Courtney Ackeifi, Randy L. Anderson, Roy W. Beck, Marc Y. Donath, Sanjoy Dutta, Joseph A. Hedrick, Stephen R. Karpen, Thomas W. Kay, Thomas Marder, Marjana Marinac, Jennifer McVean, Robert Meyer, Jeremy Puttus, Teresa Quattrin, Ruud J. Vestergen, Joseph A. Vieth, Esther Latres

Type 1 diabetes (T1D) is an autoimmune disease characterized by the destruction of insulin-producing ?-cells in the pancreas. This destruction leads to chronic hyperglycemia, necessitating lifelong insulin therapy to manage blood glucose levels. Typically diagnosed in children and young adults, T1D can, however, occur at any age. Ongoing research aims to uncover the precise mechanisms underlying T1D and to develop potential interventions. These include efforts to modulate the immune system, regenerate ?-cells, and create advanced insulin delivery systems. Emerging therapies, such as closed-loop insulin pumps, stem cell-derived ?-cell replacement and disease-modifying therapies (DMTs), offer hope for improving the quality of life for individuals with T1D and potentially moving towards a cure. Currently, there are no disease-modifying therapies approved for stage 3 T1D. Preserving ?-cell function in stage 3 T1D is associated with better clinical outcomes, including lower HbA1c and decreased risk of hypoglycemia, neuropathy, and retinopathy. Tumor Necrosis Factor alpha (TNF-?) inhibitors have demonstrated efficacy at preserving ?-cell function by measurement of C-peptide in two clinical trials in people with stage 3 T1D. However, TNF-? inhibitors have yet to be evaluated in a pivotal trial for T1D. To address the promising clinical findings of TNF-? inhibitors in T1D, Breakthrough T1D convened a panel of key opinion leaders (KOLs) in the field. The workshop aimed to outline an optimal clinical path for moving TNF-? inhibitors to a pivotal clinical trial in T1D. Here, we summarize the evidence for the beneficial use of TNF-? inhibitors in T1D and considerations for strategies collectively identified to advance TNF-? inhibitors beyond phase 2 clinical studies for stage 3 T1D.

Access the full publication here.