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The latest methods of treating type 1 diabetes, improving patients' quality of life – a review of the literature

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ABSTRACT

Introduction: Type 1 diabetes is a chronic autoimmune disease characterized by destruction of pancreatic β cells and resultant absolute insulin deficiency. Despite advances in insulin delivery systems and glucose monitoring, patients remain at risk for severe acute and chronic complications, posing a significant therapeutic challenge. Consequently, new approaches are being intensively developed, including cell-, gene-, and immunology-based therapies. One direction is pancreatic islet transplantation and the use of stem cells as a source of β cells.

Aim of the Study:. The purpose of this study is to investigate new therapies used in type diabetes that may reduce the need for exogenous insulin.

Materials and Methods: An analysis of papers available in PubMed was performed.

The following keywords were used : diabeletes mellutis type 1, immunotherapy, anti-CD3 monoclonal antibody, pancreatic islet cel transplatation, stem cell transplantation.

Basic results: Despite advances in understanding the mechanisms of autoimmune destruction of pancreatic β cells, there is no fully optimal therapy for patients with type 1 diabetes. In recent years, many modern treatment methods have been studied, including the use of anti-CD3 antibodies. In November 2022, teplizumab (an anti-CD3 antibody) was approved as a drug that, by slowing the autoimmune destruction of pancreatic β cells, prolongs endogenous insulin

production and delays the need for intensive insulin therapy. Another intensively investigated approach is pancreatic islet transplantation. The latest research results show that pancreatic islet transplantation improves glycemic control, prevents severe episodes of hypoglycemia, and makes some patients insulin-independent. In addition, results from 2024 on the first-ever transplantation of pancreatic islets derived from chemically induced pluripotent stem cells (CiPSCs) suggest that this treatment may be a personalized therapeutic strategy for patients with type 1 diabetes. However, further studies with a larger number of patients and longer follow-up periods are needed to assess the long-term safety and efficacy of this method.

Conclusion: None of the existing therapies for type 1 diabetes is entirely optimal. Rapid scientific advances and emerging stem cell transplantation technologies offer patients hope for improved quality of life through better glycemic control, prevention of severe hypoglycemic episodes, and insulin independence.

Keywords: diabeletes mellutis type 1, immunotherapy, anti-CD3 monoclonal antibody, pancreatic islet cel transplatation, stem cell transplantation.

Introduction

Type 1 diabetes is a chronic autoimmune disease in which the immune system attacks and destroys the pancreatic islet β cells responsible for insulin production. For many decades, insulin therapy has remained the mainstay of treatment, effectively compensating for the hormone deficiency, but without affecting the underlying pathogenesis of the disease. Despite advances in insulin delivery and glucose monitoring systems, patients remain at risk of serious acute and chronic complications, including hypoglycemia and diabetic ketoacidosis. In addition, for some patients, especially adolescents, type 1 diabetes is associated with chronic stress related to constant glucose monitoring. In extreme cases, the disease can lead to depression and eating disorders, such as diabulimia, which is the deliberate omission of insulin doses. In recent years, new therapeutic approaches have emerged, such as cell, gene, and immunological therapies. These therapies have the potential not only to provide the patient with insulin, but also to modify the course of the disease by influencing the autoimmune process and restoring

β cell function. One therapeutic approach is the islet transplatation, which is limited by the risk of transplant rejection. At the same time, intensive research is being conducted on the use of stem cells, including induced pluripotent stem cells (iPSCs), which can be differentiated nto β cells capable of producing insulin. Another important direction is immunomodulatory therapies, such as monoclonal antibodies, which aim to modulate the immune response and slow down the destruction of β cells. This article summarizes the current state of knowledge on these therapeutic strategies, with particular emphasis on their clinical potential and the challenges associated with their implementation.

Type 1 diabetes

In 2024, 9.2 million people were living with type 1 diabetes, 1.8 million of whom were under the age of 20. [1] Type 1 diabetes accounts for about 10% of all diabetes cases, and the incidence of this disease is increasing worldwide. In the United States, the prevalance is approximaely 1 in 300 children, and in Europe it is one of the most common chronic diseases in childhood. Based on data from 2021, scientists predict that by 2040, the number of cases will increase to 13.5-17.4 million, with the largest increase in low-income countries [2].

Pathogenesis of type 1 diabetes

Type 1 diabetes is a chronic autoimmune disease characterized by a pathogenic process that develops in several stages and usually begins long before the first clinical symptoms appear. It is likely that exposure to environmental factors that trigger an autoimmune response—such as viral infections (e.g., mumps virus, enteroviruses, rubella virus, influenza virus, EBV, CMV, HAV, poliovirus), dietary factors, alterations in the gut microbiota, toxins, or chemicals—in genetically predisposed individuals initiates the destruction of pancreatic islets mediated by mononuclear cells.

The main genetic risk factors for developing type 1 diabetes are HLA class II histocompatibility alleles, particularly the DR3-DQ2 and DR4-DQ8 haplotypes. In addition, HLA class I alleles such as HLA-A24 and HLA-B39, as well as other genes including INS, CTLA4, PTPN22, and IL2RA, influence the risk of developing the disease [3]. An example of a protective haplotype against type 1 diabetes is HLA-DRB115:01-DQA101:02-DQB1*06:02 [4].

The best-known autoantigens against which antibodies are produced are the insulin B chain peptide (11–23), glutamic acid decarboxylase (GAD65), protein tyrosine phosphatase-like protein IA-2, and zinc transporter 8 (ZnT8). Autoantigens are presented by HLA class I and II

molecules on antigen-presenting cells, leading to the activation of autoreactive CD4+ T lymphocytes. These lymphocytes stimulate B lymphocytes to produce autoantibodies and simultaneously enhance the cytotoxic activity of CD8+ T lymphocytes. CD8+ lymphocytes attack β cells through cytokines: TNF-α, IFN-γ, the Fas/FasL pathway, and perforin/granzyme-mediated mechanisms. The released cytokines activate macrophages and other elements of innate immunity, which intensifies inflammation and contributes to further destruction of β cells [3,4,5].

Treatment methods for type 1 diabetes

Immunotherapy – historical overview

The first attempts at immunotherapy in patients with type 1 diabetes were conduucted as early as 1986. Patients who had been treated with insulin for less than 2 months were given cyclosporine, an immunosuppressive drug that is a calcineurin inhibitor. The study involved 122 patients, randomly divided into two groups: one receiving cyclosporine at a dose of 7.5 mg/kg per day and the other receiving a placebo. After 9 months, the results suggested that cyclosporine could promote remission of type 1 diabetes. A side effect was a moderate increase in serum creatine levels [6]. Further studies showed that the high doses required which to achieve remission were associated with in an increased number of infections, nephrotoxicity, and a rapid return of the disease after discontinuation of treatment. In subsequent years, the effect of treatment with cyclosporine in combination with methotrexate, azathioprine, and prednisolone on the treatment of type 1 diabetes was also studied. Unfortunately, in the long term, all of these drugs were associated with adverse effects, which is why they are not commonly used in patients with type 1 diabetes [7].

Rituximab in the treatment of type 1 diabetes

Rituximab in the treatment of type 1 diabetes

T lymphocytes play a major role in the pathogenesis of type 1 diabetes, while B lymphocytes contribute through their role as antigen-presenting cells. Rituximab, an anti-CD20 antibody, selectively depletes B lymphocytes, which led to studies evaluating its efficacy in patients with type 1 diabetes.

A randomized study including 87 participants compared rituximab with placebo. The primary endpoint used to assess efficacy was C-peptide level. Results showed that in newly diagnosed patients, rituximab slowed the decline in C-peptide by approximately 8 months compared with

placebo. However, after 30 months, no significant differences in C-peptide levels, insulin requirements, or HbA1c values were observed between the two groups. Thus, rituximab demonstrates partial efficacy by delaying disease progression but does not alter disease pathophysiology [8].

Another study confirmed that rituximab slows β-cell loss, but its long-term effect on the course of the disease remains uncertain [9].

In summary, rituximab is not a therapy that reverses the pathogenesis of type 1 diabetes or enables patients to discontinue insulin treatment.

Anti-CD3 monoclonal antibody in newly diagnosed type 1 diabetes

The effect of monoclonal antibody anti- CD3 on insulin production loss in patients with type 1 diabetes began to be studied in the 2000s. In one of the first studies, 24 patients within 6 weeks of being diagnosed with type 1 diabetes were randomly assigned to receive a 14-day course of monoclonal antibody treatment or no treatment. Improved insulin production was observed in 9 of 12 patients in the treatment group compared to 2 of 12 patients in the control group, and the effect of treatment lasted for at least 12 months. The most common side effects were fever, rash, and anemia [10].

This study marked the beginning of an intensive era of research into the use of anti-CD3 monoclonal antibodies in the treatment of type 1 diabetes.

Otelixizumab

Otelixizumab is a humanized monoclonal antibody directed against the CD3 molecule on the surface of T lymphocytes. Its mechanism of action involves reducing the activity of lymphocytes that destroy pancreatic β cells. In addition, the drug promotes immune tolerance, which may help prevent further β-cell destruction. Studies have shown that otelixizumab can reduce insulin requirements in patients with newly diagnosed type 1 diabetes, with effects lasting for at least 18 months [11]. However, the use of higher doses, which are more effective in preserving pancreatic β-cell function, is limited by numerous side effects. Most patients experienced Epstein-Barr virus reactivation, cytomegalovirus infection, and cytokine release syndrome.

A multicenter, randomized, placebo-controlled trial was subsequently conducted to assess whether a lower dose of otelixizumab could preserve C-peptide secretion in patients with newly diagnosed type 1 diabetes. The study involved 281 patients who were randomly assigned to

receive either 3.1 mg otelixizumab or placebo. No significant differences were observed between the groups in metabolic parameters, including HbA1c levels, glycemic variability, and insulin requirements. More adverse events occurred in the otelixizumab group, although no EBV reactivation was detected. The lower dose of the drug was better tolerated but did not confer additional preservation of C-peptide [12]. Another study was conducted to evaluate the relationship between otelixizumab dose, safety, tolerance, and β-cell function preservation in patients with newly diagnosed type 1 diabetes. This 24-month study analyzed 28 patients, who were divided into four groups according to the cumulative dose received (9 mg, 18 mg, 27 mg, or placebo). Adverse events were observed in all treated patients, with both frequency and severity increasing in a dose-dependent manner. EBV reactivation also showed a dose-dependent pattern. After administration of 9 mg otelixizumab, C-peptide levels remained above baseline for 19 months, suggesting partial preservation of pancreatic β-cell function. Higher doses of the drug increased the risk of adverse effects and EBV reactivation without conferring additional benefits in terms of β-cell preservation [13].

Teplizumab

Teplizumab is an anti-CD3 monoclonal antibody with a mechanism of action similar to that of otelixizumab. The mechanism by which anti-CD3 antibodies modulate the pathogenesis of type 1 diabetes is only partially understood. The predominant effect of this therapy is believed to be the enhancement of regulatory T-cell (Treg) activity and the promotion of immune tolerance. Clinical trials have demonstrated that teplizumab delays progression to insulin dependence and preserves β-cell function [14,15].

In November 2022, teplizumab was approved by the U.S. Food and Drug Administration (FDA) to delay progression to stage 3 type 1 diabetes in adults and children aged 8 years and older with stage 2 type 1 diabetes. It is the first drug to be officially approved to delay the onset of overt type 1 diabetes. By slowing autoimmune destruction of pancreatic β cells, the drug prolongs endogenous insulin secretion and postpones the need for exogenous insulin therapy [16].

In 2021, a meta-analysis of eight studies evaluating the efficacy and safety of teplizumab was published. The analysis included 866 patients with type 1 diabetes and compared exogenous insulin requirements, β-cell function, HbA1c levels, and adverse events between patients treated with teplizumab and those receiving placebo. The teplizumab group demonstrated lower

insulin requirements and improved β-cell function at multiple time points (6, 12, 18, and 24 months). Glycemic control, as assessed by HbA1c, did not differ significantly between groups. The study showed that teplizumab slows β-cell destruction and prolongs endogenous insulin production without improving overall glycemic control. The most common adverse event associated with teplizumab treatment was lymphopenia [17].

In a 2020 study, researchers evaluated the association between the duration of partial clinical remission in type 1 diabetes and the coexistence of other autoimmune diseases. The results indicated that patients who experienced remission lasting more than 297 days were more likely to develop additional autoimmune diseases associated with diabetes compared with those who had a shorter remission period [18]. These findings are noteworthy because the study included a large cohort of participants consistent with the target age group for teplizumab use. Further research is warranted to determine whether teplizumab therapy is associated with an increased risk of developing other Th1-dependent autoimmune diseases. Conducting such studies is crucial to ensure patient safety and to prevent unexpected adverse effects [19].

Pancreatic islet cel transplatation- historical overview

Pancreatic islet transplantation has long been investigated as a therapeutic strategy aimed at restoring endogenous insulin production in patients with type 1 diabetes, in whom autoimmune destruction of pancreatic β cells has occurred.

In 1990, the first study was published describing a patient who was able to discontinue insulin therapy following transplantation of pancreatic islets into the portal vein [20].

A landmark study published in 2000 involved seven patients with type 1 diabetes characterized by recurrent severe hypoglycemia and unstable metabolic control. Following transplantation of an average islet mass of 11,547 ± 1,604 islet equivalents per kilogram of body weight, all patients achieved sustained insulin independence and maintained normal glycated hemoglobin (HbA1c) levels. To minimize toxicity and prevent insulin resistance, glucocorticosteroids were excluded from the immunosuppressive regimen [21].

This study demonstrated that achieving insulin independence and maintaining glycemic stability in patients with type 1 diabetes requires transplantation of a sufficiently large islet cell mass.

Allotransplantation of pancreatic islets – indications in type 1 diabetes

Allogeneic pancreatic islet transplantation is primarily performed in patients aged 18–65 years with unstable type 1 diabetes who experience poor metabolic control despite intensive insulin therapy.

The main indications for pancreatic islet transplantation include marked glycemic variability, recurrent severe hypoglycemic episodes with impaired awareness, and hyperglycemia in patients with a functioning kidney graft. Episodes of hypoglycemia in individuals with long-standing type 1 diabetes are often related to a loss of the α-cell response to hypoglycemia. In such patients, pancreatic islet transplantation can restore more physiological glycemic regulation and reduce the risk of severe hypoglycemia [22].

Another group of candidates for allogeneic islet transplantation comprises patients with multiple recurrent episodes of diabetic ketoacidosis or rapidly progressive diabetic complications [21]. Psychological disorders that significantly impair adherence to insulin therapy also represent a potential indication for transplantation. In relatively rare but severe cases of allergy or resistance to subcutaneous insulin, which pose significant therapeutic challenges, pancreatic islet transplantation should likewise be considered [23,24].

Pancreatic islet transplantation: recent clinical outcomes

In 2019, a clinical study was conducted with the primary objective of evaluating the outcomes of allogeneic pancreatic islet transplantation in patients with type 1 diabetes who had impaired hypoglycemia awareness or had previously undergone kidney transplantation. The study included 28 participants who received either islet transplantation alone or islet-after-kidney transplantation. After 5 years, 39% of patients achieved insulin independence, and after 10 years, 28% maintained insulin independence with HbA1c levels below 6.5%. Partial or full graft function was preserved in the majority of patients—82% at 5 years and 78% at 10 years. Maintenance of graft function was associated with improved metabolic control and an almost complete elimination of severe hypoglycemic episodes. The outcomes regarding insulin independence, graft survival, and metabolic control were comparable between both patient groups, with no statistically significant differences observed. In summary, pancreatic islet

transplantation provides long-term metabolic benefits, including improved glycemic control and a marked reduction in severe hypoglycemia, lasting 10 years in approximately three-quarters of patients with type 1 diabetes [25].

Observation period	Insulin independence	Transplant function
5 years	39% patients	82% patients
10 years	28% patients	78% patients

Another study aimed to identify factors associated with favorable five-year outcomes following allogeneic pancreatic islet transplantation in patients with type 1 diabetes and recurrent episodes of severe hypoglycemia. The study included 398 patients without renal failure. Four key prognostic factors were identified, which, when present simultaneously, were associated with significantly improved clinical outcomes. These factors were: recipient age >35 years, transplantation of ≥325,000 islet equivalents (IEQs), induction immunosuppression including T-cell depletion or TNF-α blockade, and maintenance immunosuppressive therapy combining mTOR and calcineurin inhibitors.

Meeting all four criteria was predictive of excellent outcomes five years post-transplant, characterized by the absence of severe hypoglycemic episodes, optimal glycemic control, and a substantial proportion of insulin-independent patients [26].

Results after 5 years:

Parameter	Patients meeting all 4 criteria
No severe episodes of hypoglycemia	95%
HbA1C < 53mmol/mol (7%)	76%
HbA_1c < 53mmol/mol 97%) 7,0 % + no SHEs	73%
Insulin independance	53%

A large study involving 1,210 patients who underwent allogeneic pancreatic islet transplantation analyzed the association between primary graft function (PGF) and 5-year clinical outcomes, including glycemic control, insulin independence, and graft loss. The results demonstrated that higher primary graft function was strongly correlated with more favorable long-term outcomes, confirming that PGF may serve as a valuable prognostic indicator for patients following islet transplantation [27].

Stem cell transplantation

Stem cell transplantation in patients with type 1 diabetes aims to restore pancreatic β cells capable of producing insulin, as well as to support regeneration and protect cells from further destruction. Various types of stem cells are used in research: mesenchymal stem cells, induced pluripotent stem cells, and hematopoietic stem cells. Mesenchymal stem cells, which have a high safety profile, are very often used in clinical trials [28].

In 2022, a study evaluated the safety and efficacy of autologous mesenchymal stem cell (MSC) transplantation in patients with newly diagnosed type 1 diabetes. The trial enrolled 21 patients and assessed hypoglycemia frequency, HbA1c levels, immune markers, and quality of life. Compared with placebo, the MSC group experienced significantly fewer hypoglycemic episodes at both level 1 (~70–55 mg/dL) and level 2 (<55–40 mg/dL), as well as a lower overall number of hypoglycemic events. Quality-of-life scores and HbA1c values also improved significantly in the MSC group. Additionally, increases in anti-inflammatory cytokines, such as IL-4 and IL-10, were observed. However, further studies are needed to confirm the long-term effects of this therapy [29].

Induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs) are pluripotent, meaning they can differentiate into any cell type in the body, including insulin-producing β cells. The number of clinical trials involving transplantation of these cells remains limited because of serious adverse effects, including the risk of neoplasia. In addition, the use of ESCs is ethically contentious due to issues related to their procurement. A key advantage of iPSCs is the potential for autologous derivation, which may reduce the need for immunosuppression in the future. However, in type 1 diabetes, the risk of an autoimmune attack on newly generated β cells persists; therefore, additional protective strategies may be required.

In 2024, the results of the first-ever transplant of pancreatic islets derived from chemically induced pluripotent stem cells (ciPSCs) in a patient with type 1 diabetes were reported. A gradual reduction in exogenous insulin requirements was observed within two weeks of the procedure, and by day 75 the patient achieved complete insulin independence, which persisted throughout the one-year follow-up. After insulin independence was achieved, fasting glucose values remained below the diagnostic thresholds for diabetes, and time in range (TIR) increased from 43.18% pre-transplant to 96.21% four months post-procedure. These findings suggest that autologous ciPSC-based therapy may represent a viable, personalized treatment strategy for

type 1 diabetes. Nevertheless, the authors emphasize the need for additional studies with larger cohorts and longer follow-up to establish long-term safety and efficacy of this metod [30].

Conclusions

The global prevalence of type 1 diabetes continues to rise, and insulin therapy—while remaining the cornerstone of management—is inevitably associated with a reduced quality of life. Over the past several decades, extensive research efforts have focused on developing therapeutic approaches that target the underlying pathophysiology of the disease and aim to restore endogenous insulin production. The first attempts at immunotherapy in patients with type 1 diabetes were undertaken as early as 1986. After nearly four decades of investigation, in 2022, the first drug—teplizumab, a monoclonal anti-CD3 antibody capable of delaying the onset of overt type 1 diabetes—was approved by the U.S. Food and Drug Administration. Allogeneic pancreatic islet transplantation has been performed for several decades, and recent studies demonstrate that this approach can achieve insulin independence, reduce the frequency of severe hypoglycemic episodes, and improve overall glycemic control. Of particular interest are the advances in islet transplantation derived from chemically induced pluripotent stem cells, as the first such procedure has yielded promising results. However, further large-scale studies are required to confirm the long-term efficacy and safety of this emerging therapy. Although no current treatment for type 1 diabetes is curative, the rapid progress in cellular, immunologic, and stem cell–based therapies offers renewed hope for achieving durable remission and improving the quality of life for patients living with this condition.

Author contributions

Conceptualization: Dominika Bąk
Methodology: Dominika Bąk
Software: Dominika Bąk
Formal analysis: Dominika Bąk
Investigation: Dominika Bąk
Resources: Dominika Bąk
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Conflict of Interest

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References

1. Type 1 Diabetes | International Diabetes Federation
2. Gregory GA, Robinson TIG, Linklater SE, Wang F, Colagiuri S, de Beaufort C, Donaghue KC; International Diabetes Federation Diabetes Atlas Type 1 Diabetes in Adults Special Interest Group; Magliano DJ, Maniam J, Orchard TJ, Rai P, Ogle GD. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. Lancet Diabetes Endocrinol. 2022 Oct;10(10):741-760. doi: 10.1016/S2213-8587(22)00218-2. Epub 2022 Sep 13. Erratum in: Lancet Diabetes Endocrinol. 2022 Nov;10(11):e11. doi: 10.1016/S2213-8587(22)00280-7. PMID: 36113507.
3. Zajec A, Trebušak Podkrajšek K, Tesovnik T, Šket R, Čugalj Kern B, Jenko Bizjan B, Šmigoc Schweiger D, Battelino T, Kovač J. Pathogenesis of Type 1 Diabetes: Established Facts and New Insights. Genes (Basel). 2022 Apr 16;13(4):706. doi: 10.3390/genes13040706. PMID: 35456512; PMCID: PMC9032728.
4. Giwa AM, Ahmed R, Omidian Z, Majety N, Karakus KE, Omer SM, Donner T, Hamad ARA. Current understandings of the pathogenesis of type 1 diabetes: Genetics to environment. World J Diabetes. 2020 Jan 15;11(1):13-25. doi: 10.4239/wjd.v11.i1.13. PMID: 31938470; PMCID: PMC6927819

5. Burrack AL, Martinov T, Fife BT. T Cell-Mediated Beta Cell Destruction: Autoimmunity and Alloimmunity in the Context of Type 1 Diabetes. Front Endocrinol (Lausanne). 2017 Dec 5;8:343. doi: 10.3389/fendo.2017.00343. PMID: 29259578; PMCID: PMC5723426.
6. Feutren G, Papoz L, Assan R, Vialettes B, Karsenty G, Vexiau P, Du Rostu H, Rodier M, Sirmai J, Lallemand A, et al. Cyclosporin increases the rate and length of remissions in insulin-dependent diabetes of recent onset. Results of a multicentre double-blind trial. Lancet. 1986 Jul 19;2(8499):119-24. doi: 10.1016/s0140-6736(86)91943-4. PMID: 2873396.
7. Jeun R. Immunotherapies for prevention and treatment of type 1 diabetes. Immunotherapy. 2025 Feb;17(3):201-210. doi: 10.1080/1750743X.2025.2473311. Epub 2025 Mar 4. PMID: 40033931; PMCID: PMC11951698.
8. Pescovitz MD, Greenbaum CJ, Bundy B, Becker DJ, Gitelman SE, Goland R, Gottlieb PA, Marks JB, Moran A, Raskin P, Rodriguez H, Schatz DA, Wherrett DK, Wilson DM, Krischer JP, Skyler JS; Type 1 Diabetes TrialNet Anti-CD20 Study Group. B-lymphocyte depletion with rituximab and β-cell function: two-year results. Diabetes Care. 2014 Feb;37(2):453-9. doi: 10.2337/dc13-0626. Epub 2013 Sep 11. PMID: 24026563; PMCID: PMC3898764.
9. Herold KC, Pescovitz MD, McGee P, Krause-Steinrauf H, Spain LM, Bourcier K, Asare A, Liu Z, Lachin JM, Dosch HM; Type 1 Diabetes TrialNet Anti-CD20 Study Group. Increased T cell proliferative responses to islet antigens identify clinical responders to anti-CD20 monoclonal antibody (rituximab) therapy in type 1 diabetes. J Immunol. 2011 Aug 15;187(4):1998-2005. doi: 10.4049/jimmunol.1100539. Epub 2011 Jul 20. PMID: 21775681; PMCID: PMC3150302.
10. Killestein J. Anti-CD3 monoclonal antibody in new-onset type 1 diabetes mellitus. N Engl J Med. 2002 Oct 3;347(14):1116-7; author reply 1116-7. doi: 10.1056/NEJM200210033471416. PMID: 12362018.
11. Hale G, Rebello P, Al Bakir I, Bolam E, Wiczling P, Jusko WJ, Vandemeulebroucke E, Keymeulen B, Mathieu C, Ziegler AG, Chatenoud L, Waldmann H. Pharmacokinetics and antibody responses to the CD3 antibody otelixizumab used in the treatment of type 1 diabetes. J Clin Pharmacol. 2010 Nov;50(11):1238-48. doi: 10.1177/0091270009356299. Epub 2010 Feb 10. PMID: 20147616.

12. Aronson R, Gottlieb PA, Christiansen JS, Donner TW, Bosi E, Bode BW, Pozzilli P; DEFEND Investigator Group. Low-dose otelixizumab anti-CD3 monoclonal antibody DEFEND-1 study: results of the randomized phase III study in recent-onset human type 1 diabetes. Diabetes Care. 2014 Oct;37(10):2746-54. doi: 10.2337/dc13-0327. Epub 2014 Jul 10. PMID: 25011949; PMCID: PMC4392937.
13. Keymeulen B, van Maurik A, Inman D, Oliveira J, McLaughlin R, Gittelman RM, Roep BO, Gillard P, Hilbrands R, Gorus F, Mathieu C, Van de Velde U, Wisniacki N, Napolitano A. A randomised, single-blind, placebo-controlled, dose-finding safety and tolerability study of the anti-CD3 monoclonal antibody otelixizumab in new-onset type 1 diabetes. Diabetologia. 2021 Feb;64(2):313-324. doi: 10.1007/s00125-020-05317-y. Epub 2020 Nov 4. PMID: 333145642; PMCID: PMC7801303.
14. Thakkar S, Chopra A, Nagendra L, Kalra S, Bhattacharya S. Teplizumab in Type 1 Diabetes Mellitus: An Updated Review. touchREV Endocrinol. 2023 Nov;19(2):22-30. doi: 10.17925/EE.2023.19.2.7. Epub 2023 Oct 6. PMID: 38187075; PMCID: PMC10769466.
15. Sims EK, Bundy BN, Stier K, Serti E, Lim N, Long SA, Geyer SM, Moran A, Greenbaum CJ, Evans-Molina C, Herold KC; Type 1 Diabetes TrialNet Study Group. Teplizumab improves and stabilizes beta cell function in antibody-positive high-risk individuals. Sci Transl Med. 2021 Mar 3;13(583):eabc8980. doi: 10.1126/scitranslmed.abc8980. PMID: 33658358; PMCID: PMC8610022
16. tzield-en
17. Nourelden AZ, Elshanbary AA, El-Sherif L, Benmelouka AY, Rohim HI, Helmy SK, Sayed MK, Ismail A, Ali AS, Ragab KM, Zaazouee MS. Safety and Efficacy of Teplizumab for Treatment of Type One Diabetes Mellitus: A Systematic Review and Meta-Analysis. Endocr Metab Immune Disord Drug Targets. 2021;21(10):1895-1904. doi: 10.2174/1871530320999201209222921. PMID: 33302842.
18. Ozen G, Zanfardino A, Confetto S, Piscopo A, Casaburo F, Tinto N, Iafusco F, Ozen G, Miraglia Del Giudice E, Tasar MA, Yilmaz A, Iafusco D. The Association of Autoimmune Diseases with Type 1 Diabetes Mellitus in Children Depends Also by the Length of Partial Clinical Remission Phase (Honeymoon). Int J Endocrinol. 2020 Jan 4;2020:2630827. doi: 10.1155/2020/2630827. PMID: 32215008; PMCID: PMC7082813.

19. Ozen G, Iafusco D. Teplizumab: Is It a Milestone for Type 1 Diabetes or a Risk Factor for Other Autoimmune Diseases in the Long Term? Clin Diabetes. 2024 Spring;42(2):314-315. doi: 10.2337/cd23-0073. Epub 2023 Dec 15. PMID: 38666196; PMCID: PMC11040010.
20. Scharp DW, Lacy PE, Santiago JV, McCullough CS, Weide LG, Falqui L, Marchetti P, Gingerich RL, Jaffe AS, Cryer PE, et al. Insulin independence after islet transplantation into type I diabetic patient. Diabetes. 1990 Apr;39(4):515-8. doi: 10.2337/diab.39.4.515. PMID: 2108071.
21. Rickels MR, Robertson RP. Pancreatic Islet Transplantation in Humans: Recent Progress and Future Directions. Endocr Rev. 2019 Apr 1;40(2):631-668. doi: 10.1210/er.2018-00154. PMID: 30541144; PMCID: PMC6424003.
22. Shapiro AM, Lakey JR, Ryan EA, Korbutt GS, Toth E, Warnock GL, Kneteman NM, Rajotte RV. Islet transplantation in seven patients with type 1 diabetes mellitus using a glucocorticoid-free immunosuppressive regimen. N Engl J Med. 2000 Jul 27;343(4):230-8. doi: 10.1056/NEJM200007273430401. PMID: 10911004.
23. Choudhary P, Rickels MR, Senior PA, Vantyghem MC, Maffi P, Kay TW, Keymeulen B, Inagaki N, Saudek F, Lehmann R, Hering BJ. Evidence-informed clinical practice recommendations for treatment of type 1 diabetes complicated by problematic hypoglycemia. Diabetes Care. 2015 Jun;38(6):1016-29. doi: 10.2337/dc15-0090. PMID: 25998294; PMCID: PMC4439532.
24. Sordi V, Monaco L, Piemonti L. Cell Therapy for Type 1 Diabetes: From Islet Transplantation to Stem Cells. Horm Res Paediatr. 2023;96(6):658-669. doi: 10.1159/000526618. Epub 2022 Aug 30. PMID: 36041412.
25. Vantyghem MC, Chetboun M, Gmyr V, Jannin A, Espiard S, Le Mapihan K, Raverdy V, Delalleau N, Machuron F, Hubert T, Frimat M, Van Belle E, Hazzan M, Pigny P, Noel C, Caiazzo R, Kerr-Conte J, Pattou F; Members of the Spanish Back Pain Research Network Task Force for the Improvement of Inter-Disciplinary Management of Spinal Metastasis. Ten-Year Outcome of Islet Alone or Islet After Kidney Transplantation in Type 1 Diabetes: A Prospective Parallel-Arm Cohort Study. Diabetes Care. 2019 Nov;42(11):2042-2049. doi: 10.2337/dc19-0401. Erratum in: Diabetes Care. 2020 May;43(5):1164. doi: 10.2337/dc20-er05. PMID: 31615852.

26. Hering BJ, Ballou CM, Bellin MD, Payne EH, Kandeel F, Witkowski P, Alejandro R, Rickels MR, Barton FB. Factors associated with favourable 5 year outcomes in islet transplant alone recipients with type 1 diabetes complicated by severe hypoglycaemia in the Collaborative Islet Transplant Registry. Diabetologia. 2023 Jan;66(1):163-173. doi: 10.1007/s00125-022-05804-4. Epub 2022 Oct 6. PMID: 36201044; PMCID: PMC10355148.
27. Chetboun M, Drumez E, Ballou C, Maanaoui M, Payne E, Barton F, Kerr-Conte J, Vantyghem MC, Piemonti L, Rickels MR, Labreuche J, Pattou F; Collaborative Islet Transplant Registry (CITR) Investigators study group. Association between primary graft function and 5-year outcomes of islet allogeneic transplantation in type 1 diabetes: a retrospective, multicentre, observational cohort study in 1210 patients from the Collaborative Islet Transplant Registry. Lancet Diabetes Endocrinol. 2023 Jun;11(6):391-401. doi: 10.1016/S2213-8587(23)00082-7. Epub 2023 Apr 24. PMID: 37105208; PMCID: PMC10388704.
28. Ra JC, Shin IS, Kim SH, Kang SK, Kang BC, Lee HY, Kim YJ, Jo JY, Yoon EJ, Choi HJ, Kwon E. Safety of intravenous infusion of human adipose tissue-derived mesenchymal stem cells in animals and humans. Stem Cells Dev. 2011 Aug;20(8):1297-308. doi: 10.1089/scd.2010.0466. Epub 2011 Mar 17. PMID: 21303266.
29. Izadi M, Sadr Hashemi Nejad A, Moazenchi M, Masoumi S, Rabbani A, Kompani F, Hedayati Asl AA, Abbasi Kakroodi F, Jaroughi N, Mohseni Meybodi MA, Setoodeh A, Abbasi F, Hosseini SE, Moeini Nia F, Salman Yazdi R, Navabi R, Hajizadeh-Saffar E, Baharvand H. Mesenchymal stem cell transplantation in newly diagnosed type-1 diabetes patients: a phase I/II randomized placebo-controlled clinical trial. Stem Cell Res Ther. 2022 Jun 20;13(1):264. doi: 10.1186/s13287-022-02941-w. PMID: 35725652; PMCID: PMC9208234.
30. Wang S, Du Y, Zhang B, Meng G, Liu Z, Liew SY, Liang R, Zhang Z, Cai X, Wu S, Gao W, Zhuang D, Zou J, Huang H, Wang M, Wang X, Wang X, Liang T, Liu T, Gu J, Liu N, Wei Y, Ding X, Pu Y, Zhan Y, Luo Y, Sun P, Xie S, Yang J, Weng Y, Zhou C, Wang Z, Wang S, Deng H, Shen Z. Transplantation of chemically induced pluripotent stem-cell-derived islets under abdominal anterior rectus sheath in a type 1 diabetes patient. Cell. 2024 Oct 31;187(22):6152-6164.e18. doi: 10.1016/j.cell.2024.09.004. Epub 2024 Sep 25. PMID: 39326417.