Understanding Stem Cell Therapy for Type 2 Diabetes

A Patient Guide from Auragens

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Advancing Regenerative Medicine:
Treatments & Empathy Amplified by Science and Technology

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Welcome

Living with Type 2 diabetes is a daily commitment — to monitoring your blood sugar, managing your medications, adjusting your diet, and staying alert to the long-term complications that can quietly develop over time. It can be exhausting, and for many people, even their best efforts are not enough to stop the disease from progressing.

If you are reading this guide, you may be exploring whether regenerative medicine — and specifically, therapy with human umbilical cord-derived mesenchymal stem cells (hUC-MSCs) — could play a role in your care. We want to help you understand what the science currently shows, what this therapy may and may not offer, and how Auragens approaches your care.

This guide is an educational resource. It is designed to prepare you for an informed conversation with the Auragens medical team and your own physicians. It does not replace medical advice, and it does not promise outcomes. What it does offer is an honest, evidence-based, and compassionate look at where the science stands today — and what it may mean for you.

1. Understanding

What Is Type 2 Diabetes?

Type 2 diabetes mellitus (T2DM) is one of the most common chronic metabolic conditions in the world. At its core, it is a disorder of how your body handles glucose — the sugar that fuels your cells. In a healthy body, the pancreas produces a hormone called insulin that acts like a key, unlocking cells so glucose can enter and be used for energy. In Type 2 diabetes, two things go wrong at the same time: the body's cells become resistant to insulin's signal, and the pancreas gradually loses its ability to produce enough insulin to compensate. The result is persistently elevated blood sugar — a state that, over time, damages blood vessels, nerves, kidneys, eyes, and the heart [1, 2].

Type 2 diabetes is closely linked to obesity, physical inactivity, and genetic predisposition, but it affects people across a wide range of body types and backgrounds. It is distinct from Type 1 diabetes, which is an autoimmune condition in which the immune system destroys insulin-producing cells. In Type 2 diabetes, those cells — called beta cells — are initially present but progressively impaired and lost over the course of the disease [1].

How Does It Progress?

The progression of Type 2 diabetes is gradual and often silent in its early stages. It typically begins with insulin resistance — a state in which the body's muscle, fat, and liver cells do not respond normally to insulin. To compensate, the pancreas works harder and produces more insulin. For years, this compensatory effort can keep blood sugar relatively controlled. But over time, the beta cells become exhausted. They lose their ability to secrete insulin effectively, and eventually some are lost entirely [1, 2].

This progressive beta cell decline is the central challenge of Type 2 diabetes. It explains why the disease tends to worsen over time even in patients who are diligent about their treatment — and why so many patients who initially managed their diabetes with lifestyle changes or a single oral medication eventually require multiple medications or insulin [1].

Several biological processes accelerate this decline:

- **Chronic low-grade inflammation:** Elevated levels of inflammatory proteins — including TNF-alpha and IL-1beta — are present in the blood and tissues of people with Type 2 diabetes. These inflammatory signals interfere with insulin signaling and directly damage beta cells [3].
- **Oxidative stress:** Excess glucose and fat metabolism generate harmful molecules called reactive oxygen species. These damage beta cells, impair insulin secretion, and worsen insulin resistance throughout the body [4].
- **Glucotoxicity and lipotoxicity:** Chronically elevated blood sugar and fatty acids create a toxic environment within the pancreatic islets, accelerating beta cell dysfunction and death [1].
- **ER stress:** Beta cells are among the most metabolically active cells in the body. Under sustained demand, the cellular machinery responsible for protein folding becomes overwhelmed, triggering a stress response that can lead to beta cell apoptosis (programmed cell death) [1].

Major Symptoms and Burdens

Type 2 diabetes can be present for years before a person experiences obvious symptoms. When symptoms do appear, they may include increased thirst and urination, fatigue, blurred vision, slow-healing wounds, and recurrent infections. Over the long term, uncontrolled diabetes can lead to:

- **Cardiovascular disease** — the leading cause of death in people with T2DM
- **Diabetic kidney disease (nephropathy)** — a leading cause of kidney failure
- **Peripheral neuropathy** — nerve damage causing pain, numbness, or weakness, especially in the feet
- **Retinopathy** — damage to the blood vessels of the retina, a leading cause of blindness
- **Diabetic foot complications** — including ulcers and, in severe cases, amputation

The physical, emotional, and economic burden of Type 2 diabetes is substantial. Managing this condition requires lifelong vigilance and places significant demands on patients, families, and healthcare systems alike [2].

Current Standard Treatments

Today's standard treatments for Type 2 diabetes include a range of medications, each targeting a different aspect of the disease:

- **Metformin** is typically the first medication prescribed. It reduces the liver's glucose production and modestly improves insulin sensitivity. It is generally safe, well tolerated, and has a long track record — but it does not stop the progressive loss of beta cell function [2].
- **Sulfonylureas** stimulate the pancreas to release more insulin. They are effective in the short term but carry a risk of low blood sugar (hypoglycemia) and may accelerate beta cell exhaustion over time [1].
- **GLP-1 receptor agonists** are a newer class of injectable medications that enhance insulin secretion, reduce appetite, and have shown cardiovascular and kidney benefits in clinical trials. They are an important advance, but they are not universally accessible, do not restore lost beta cell mass, and are not effective for all patients [2].
- **SGLT2 inhibitors** lower blood sugar by causing the kidneys to excrete excess glucose in the urine. They also offer heart and kidney protection in high-risk patients, but carry risks including genital infections and, in some settings, a rare condition called euglycemic ketoacidosis [2].
- **Insulin therapy** remains essential for many patients with advanced disease. It is highly effective at controlling blood sugar but requires careful dosing, carries a risk of hypoglycemia, and does not restore the body's own insulin-producing capacity [1].

The Limitations of Current Treatments

Current medications are genuinely valuable. They reduce complications, improve quality of life, and in many cases extend life. But they share a fundamental limitation: **they manage the consequences of beta cell loss rather than addressing the loss itself** [1, 2].

No currently approved medication reliably restores lost beta cell mass, reverses insulin resistance at its inflammatory root, or durably arrests the progression of the disease in most patients. As beta cell function continues to decline, treatment regimens typically become more complex, more burdensome, and more expensive. A significant proportion of patients — even those who follow their treatment plans carefully — still develop serious complications over time [1, 2].

This gap between what current therapy can offer and what patients truly need has motivated researchers to explore regenerative approaches — therapies designed not merely to control blood sugar, but to address the underlying biological processes that drive the disease.

2. What Are hUC-MSCs from Wharton's Jelly?

Mesenchymal Stem Cells: A Brief Introduction

Mesenchymal stem cells (MSCs) are a type of adult stem cell found in several tissues throughout the body, including bone marrow, fat tissue, and the umbilical cord. They are not the same as embryonic stem cells — they do not come from embryos and do not carry the same ethical concerns. MSCs have attracted significant scientific interest because of their remarkable ability to communicate with the immune system, reduce inflammation, support tissue repair, and secrete a wide range of biologically active molecules that influence the health of surrounding cells [5].

Importantly, MSCs do not work primarily by becoming new cells themselves. Instead, they act largely as sophisticated signaling hubs — releasing proteins, growth factors, and tiny vesicles called exosomes that instruct the body's own cells to behave in healthier, more balanced ways. This paracrine (neighbor-to-neighbor) communication is now understood to be the primary mechanism behind the therapeutic effects observed in research settings [5].

Why Wharton's Jelly?

MSCs can be sourced from many tissues, but umbilical cord tissue — specifically a gelatinous connective tissue inside the cord called **Wharton's Jelly** — has emerged as one of the most promising sources for clinical use. Here is why:

- **Abundance and accessibility:** The umbilical cord is routinely discarded after birth. With appropriate donor consent, it can be collected ethically, without any procedure that harms the donor or the newborn [5].
- **Youth and potency:** Wharton's Jelly MSCs (WJ-MSCs) are derived from a very early developmental tissue. Compared to MSCs from older donors, they tend to be more proliferative, more potent in their immunomodulatory effects, and less likely to carry the accumulated damage associated with aging [5].
- **Low immunogenicity:** One of the most clinically significant properties of hUC-MSCs is their low immunogenic profile — meaning they are unlikely to trigger an immune rejection response in the recipient. This makes them suitable for use as an **allogeneic therapy** (cells from a donor used in a different person), without the need for immune-matching or long-term immunosuppression [5].

- **Scalability:** Because WJ-MSC lines can be expanded in the laboratory from a single umbilical cord donation, they can be produced in quantities sufficient for clinical use, supporting consistent and standardized treatment [5].

From Donation to Treatment: The Journey of hUC-MSCs

The process of preparing hUC-MSCs for clinical use involves multiple carefully controlled steps:

1. **Donor screening:** Umbilical cord donors are thoroughly screened for infectious diseases, genetic conditions, and other health factors before donation is accepted. This process mirrors the rigorous standards applied to blood and organ donation.
2. **Tissue processing:** The Wharton's Jelly is carefully separated from the cord and processed under sterile laboratory conditions to isolate the MSC population.
3. **Cell expansion:** The isolated cells are grown (expanded) in controlled laboratory environments to produce the quantities needed for treatment.
4. **Quality control:** Expanded cells undergo extensive testing to confirm their identity, purity, potency, and freedom from contamination before being approved for use.
5. **Cryopreservation:** Validated cell batches are cryopreserved (frozen) at ultra-low temperatures to preserve viability and allow for safe storage and transport.
6. **Pre-treatment preparation:** Prior to infusion, cells are thawed and prepared according to standardized protocols to ensure maximum viability and safety at the time of administration.

Every step in this process is governed by strict quality standards designed to protect patients and ensure consistency from one treatment to the next.

🏆 Why Auragens: AABB Accreditation — The Gold Standard in Cellular Therapy

Auragens Stem Cell Center is proud to be AABB accredited — a critical distinction that sets us apart from unaccredited clinics.

What is AABB Accreditation?

AABB (Association for Advancement of Blood and Biotherapies) is the internationally recognized leader in setting quality and safety standards for cellular therapies. AABB is a deemed status organization by the FDA and AABB accreditation represents the gold standard in the field — the most rigorous, comprehensive certification available for facilities that process and administer cellular products.

What Does AABB Accreditation Mean for You?

When you choose an AABB-accredited center like Auragens, you can trust that we meet the highest international standards in:

- **Cell Processing Excellence:** Our laboratory protocols follow strict, validated procedures ensuring every cell product meets pharmaceutical-grade quality specifications.
- **Donor Screening & Safety:** Comprehensive screening protocols ensure all donor tissue is thoroughly tested and meets stringent safety criteria.
- **Laboratory Practices:** Our facilities, equipment, and processes undergo regular inspection and must meet exacting standards for sterility, environmental control, and quality assurance.
- **Patient Safety:** From cell arrival through administration and follow-up, every step is designed and monitored to protect your safety.
- **Staff Expertise:** Our team maintains specialized training and competency requirements specific to cellular therapy.
- **Traceability & Documentation:** Complete tracking and documentation of every cell product ensures full accountability.
- **Continuous Quality Improvement:** Regular audits, proficiency testing, and quality reviews.

Why This Matters

The field of stem cell therapy is rapidly growing, but not all clinics meet the same standards. Many facilities operate without independent accreditation or oversight. AABB accreditation means an external, U.S., FDA, expert organization has thoroughly inspected and validated our practices — giving you independent verification, proven quality systems, and genuine peace of mind. When you choose Auragens, you're choosing a center that has been independently verified to meet the most stringent international standards for cellular therapy quality and safety.

AABB accreditation is not easy to achieve or maintain — it requires significant investment in infrastructure, training, quality systems, and ongoing compliance. We've made this commitment because you deserve nothing less than the highest standard of care.

3. How hUC-MSCs May Help with Type 2 Diabetes

The biology of Type 2 diabetes — chronic inflammation, progressive beta cell loss, impaired insulin signaling, and oxidative tissue damage — maps closely onto several of the key mechanisms through which hUC-MSCs have been shown to act in preclinical and early clinical research. This section explains those mechanisms in plain language, with reference to the studies that support them.

It is important to note that this therapy is **investigational**. The mechanisms described below are supported by laboratory and animal studies, and in some cases by early human trials, but they have not been definitively proven in large-scale clinical trials. Research is ongoing.

3.1 Immunomodulation: Rebalancing the Immune System

Chronic low-grade inflammation is not just a symptom of Type 2 diabetes — it is one of its drivers. Inflammatory signals from immune cells damage beta cells directly and interfere with insulin signaling throughout the body. One of the most well-studied properties of hUC-MSCs is their ability to shift the immune system toward a less inflammatory, more regulatory state.

Research has shown that hUC-MSCs can reprogram macrophages — key immune cells — away from a pro-inflammatory state (called M1) toward an anti-inflammatory, tissue-supportive state (called M2). In studies of diabetic animal models, this shift in macrophage behavior in fat tissue and in the pancreatic islets was associated with reduced inflammation and improved insulin sensitivity [6].

hUC-MSCs also appear to work through the spleen, a central hub of immune regulation. When infused intravenously, MSCs preferentially home to the spleen, where they stimulate the production of regulatory T cells (Tregs) and the anti-inflammatory cytokine IL-10. This spleen-mediated immune rebalancing then ripples outward to reduce inflammation in metabolic tissues throughout the body [7].

3.2 Anti-Inflammatory Effects: Targeting the NLRP3 Inflammasome

A specific inflammatory pathway called the **NLRP3 inflammasome** has been identified as a key contributor to beta cell damage and insulin resistance in Type 2 diabetes. When activated, this pathway triggers the release of potent inflammatory molecules — including IL-1beta and IL-18 — that impair insulin receptor signaling and promote beta cell death.

Studies have demonstrated that hUC-MSCs can suppress NLRP3 inflammasome activation in diabetic models, reducing the levels of these harmful inflammatory molecules, restoring insulin receptor downstream signaling, and improving glucose tolerance [8]. This targeted anti-inflammatory effect represents a potentially meaningful way to interrupt one of the key cycles that drives disease progression in T2DM.

3.3 Beta Cell Protection and Preservation

Protecting the beta cells that remain is one of the most important goals in managing Type 2 diabetes. Research suggests that hUC-MSCs may support beta cell health through several complementary mechanisms:

- By reducing islet inflammation (via macrophage polarization and NLRP3 suppression), hUC-MSCs create a more protective environment around the beta cells, reducing the immune-mediated damage that contributes to their loss [9, 8].
- Wharton's Jelly MSCs engineered to overexpress a signaling peptide called apelin demonstrated increased beta cell proliferation, higher insulin and C-peptide levels,

and reduced inflammatory cytokines in diabetic rat models — suggesting that MSC-delivered trophic factors may support beta cell mass recovery [10].

- hUC-MSC-derived exosomes (discussed in section 4.5) have been shown to reduce beta cell apoptosis and preserve islet structure in preclinical models [11].

These findings suggest that hUC-MSCs may help preserve — and potentially support the recovery of — residual beta cell function, particularly in patients who still retain some insulin-producing capacity.

3.4 Improving Insulin Sensitivity

Beyond protecting the pancreas, hUC-MSCs may also help the body's tissues respond more effectively to insulin. Studies in diabetic animal models have shown that hUC-MSC transplantation can improve insulin sensitivity in skeletal muscle by modulating key intracellular signaling pathways — specifically, the PI3K/Akt and ERK/MAPK pathways that regulate how cells take up glucose in response to insulin [12].

By restoring the balance of these signaling cascades, hUC-MSCs may help break the cycle of insulin resistance that is central to Type 2 diabetes — not just by reducing inflammation, but by directly normalizing the molecular machinery through which insulin acts.

3.5 Exosome Signaling: The Paracrine Effect

A growing body of research suggests that much of the therapeutic benefit of hUC-MSCs may be mediated not by the cells themselves, but by the tiny vesicles they release — called **exosomes** or small extracellular vesicles (sEVs). These nanoscale packages carry proteins, lipids, and microRNAs (small regulatory molecules) that can enter recipient cells and reprogram their behavior.

In Type 2 diabetes research, hUC-MSC-derived exosomes have demonstrated several promising effects:

- **Reversing insulin resistance:** Intravenously administered hUC-MSC exosomes restored key insulin signaling proteins (IRS-1 and AKT phosphorylation), promoted the movement of glucose transporter GLUT4 to the cell surface in muscle tissue, increased glycogen storage in the liver, and reduced beta cell apoptosis in diabetic rat models [11].
- **Improving glucose control:** Low doses of hUC-MSC small extracellular vesicles improved glucose tolerance, reduced HbA1c, and protected the pancreas, liver, and kidneys in preclinical models — suggesting that the cell-free secretome of MSCs may carry meaningful therapeutic potential [13].
- **Reversing beta cell dedifferentiation:** MSC-derived exosomal microRNAs (such as miR-146a) have been shown to reverse a process called beta cell dedifferentiation — in which beta cells lose their identity and insulin-producing function — through specific molecular signaling cascades [14].

The exosome research is particularly exciting because it suggests that hUC-MSCs may exert their effects through a distributed, systemic signaling network — one that does not require the cells to permanently engraft in any tissue.

3.6 Oxidative Stress Reduction

Oxidative stress — the accumulation of reactive oxygen species that damage cells and tissues — is a major contributor to both beta cell loss and peripheral insulin resistance in Type 2 diabetes. hUC-MSCs and their secreted products have been associated with reductions in oxidative stress markers in preclinical models, potentially through the modulation of antioxidant pathways within target tissues [4, 13]. This is an area of active investigation, and the precise molecular mechanisms in human disease remain under study.

4. Clinical Evidence and Research Findings

The State of the Evidence

Research into hUC-MSC therapy for Type 2 diabetes has advanced meaningfully over the past decade. The evidence base now includes randomized controlled trials, prospective cohort studies, safety evaluations, and systematic reviews — a level of rigor that distinguishes this field from many other areas of regenerative medicine. At the same time, it is important to be honest: the evidence is still early, most trials have been conducted at single centers with modest sample sizes, and larger confirmatory studies are needed before definitive conclusions can be drawn.

What follows is a fair and transparent summary of what the research currently shows.

4.1 Blood Sugar Control (HbA1c)

The most rigorous human evidence comes from a randomized, double-blind, placebo-controlled Phase II trial by Zang and colleagues, published in *Stem Cells Translational Medicine* in 2023. In this trial, adults with Type 2 diabetes received repeated intravenous infusions of human umbilical cord-derived MSCs or placebo. At 48 weeks, the UC-MSC group achieved a mean HbA1c reduction of **-1.36%** compared to **-0.51%** in the placebo group. At an earlier assessment at 9 weeks, the difference was even more pronounced (-1.79% vs. -0.96%) [15].

These differences are clinically meaningful. A reduction of approximately 1% in HbA1c is associated with a significant decrease in the risk of diabetes-related complications. The fact that this was achieved in a placebo-controlled, blinded trial adds important credibility to the finding.

An earlier randomized, double-blind, placebo-controlled Phase II trial from the same research program (Zang et al., *Stem Cell Research & Therapy*, 2022) reported similar

directional findings, with UC-MSC recipients showing greater HbA1c reductions and improved glycemic outcomes compared to placebo [16].

A systematic review and meta-analysis examining stem cell therapy across diabetes studies (including both Type 1 and Type 2) confirmed that MSC-based therapies were associated with meaningful improvements in glycemic markers across the pooled evidence base, while also noting the heterogeneity of the available studies [17].

4.2 Time in Range and Daily Glucose Patterns

Beyond average blood sugar (HbA1c), the Phase II trial by Zang et al. (2023) also assessed **time in range (TIR)** — the proportion of time a patient spends with blood glucose in a healthy target range. This metric, measured by continuous glucose monitoring, is increasingly recognized as a more meaningful indicator of daily diabetes management than HbA1c alone.

At 9 weeks, **59.5%** of UC-MSC recipients achieved a TIR of >=70%, compared to **27.8%** of placebo recipients. At 48 weeks, **43.2%** of UC-MSC recipients maintained TIR >=70%, compared to **11.1%** of placebo recipients. The absolute improvement in TIR at 48 weeks was 21.36% in the UC-MSC group versus 6.32% in the placebo group [15].

These findings suggest that UC-MSC therapy may help patients spend more of each day in a healthy glucose range — reducing both the highs and lows that contribute to complications and affect quality of life.

4.3 Insulin Requirements

Several clinical reports have documented reductions in insulin requirements following UC-MSC therapy. In the Phase II program, analyses of predictive factors found that many responders were able to reduce their insulin doses substantially — in some cases to approximately half their baseline requirements [18]. Earlier randomized trial data from the same program also documented insulin dose decreases versus placebo [16].

It is important to note that insulin reduction was not universal. Response varied between individuals, and insulin sparing was more pronounced in patients with certain baseline characteristics (discussed below in Section 5.5).

4.4 Beta Cell Function (C-Peptide)

C-peptide is a protein released by the pancreas alongside insulin and serves as a direct measure of the body's own insulin production. It is an important indicator of residual beta cell function.

In the UC-MSC clinical program, C-peptide levels — specifically the area under the curve (AUC) of stimulated C-peptide — were identified as an **independent predictor of**

therapeutic response. Patients with higher baseline C-peptide levels (indicating more residual beta cell function) tended to respond more favorably to UC-MSC therapy [15, 18].

C-peptide changes after treatment were heterogeneous — some patients showed increases, while others did not. This variability reflects the biological reality that patients at different stages of beta cell loss may respond differently to the therapy. It also suggests that UC-MSC therapy may be most beneficial in patients who still retain meaningful residual beta cell capacity.

4.5 Who Responds Best? Variability and Predictive Factors

One of the most consistent findings across the UC-MSC clinical literature is that **response is heterogeneous** — not all patients benefit equally. Wang and colleagues published a dedicated analysis of predictive factors for therapeutic efficacy in the UC-MSC T2DM program (*Cytotherapy*, 2024), identifying baseline C-peptide as an independent predictor of response and highlighting the importance of patient selection for optimizing outcomes [18].

Other factors that may influence response include disease duration, baseline HbA1c, degree of insulin resistance, and concurrent medications. Research is ongoing to refine patient selection criteria and identify which individuals are most likely to benefit from this therapy.

4.6 Complications-Focused Studies

Beyond glycemic outcomes, UC-MSC research has begun to address the complications of Type 2 diabetes directly:

- A Phase I clinical trial of Wharton's Jelly MSC transplantation in patients with **critical limb ischemia** related to T2DM reported improvements in pain scores, walking time, and wound healing, with no major safety signals in this small cohort (Ashoobi et al., *Cell and Tissue Research*, 2024) [19].
- A Phase I/II randomized controlled trial of hUC-MSC-derived secretome (cell-free products) for **diabetic foot ulcers** reported complete ulcer healing in the treated group, with good tolerability and no significant adverse events (Jafar et al., *Stem Cell Research & Therapy*, 2025) [20].

These early findings suggest that the therapeutic potential of hUC-MSC therapy in T2DM may extend beyond blood sugar control to the tissue repair and vascular challenges that cause the most serious complications.

4.7 Longer-Term Follow-Up

One randomized controlled study examined the long-term outcomes of a combination cell therapy (bone marrow MSCs plus mononuclear cells) in Type 2 diabetes patients over an 8-year follow-up period. While this study used a different cell source than hUC-MSCs, it

provides important conceptual evidence that MSC-based therapies may offer durable metabolic benefits in some patients — while also confirming that heterogeneous responses persist over time (Wu et al., *Stem Cell Research & Therapy*, 2024) [21].

4.8 Limitations of the Current Evidence

Transparency requires acknowledging what the evidence does not yet establish:

- **Sample sizes are modest.** Most randomized UC-MSC trials in T2DM have enrolled tens to low hundreds of patients. Larger, multi-center trials are needed to confirm findings.
- **Most trials are single-center.** Replication across different clinical settings and patient populations is necessary to establish generalizability.
- **Long-term data for UC-MSCs specifically are limited.** The 8-year follow-up data cited above used a different cell source. Long-term outcomes for hUC-MSC therapy in T2DM remain under investigation.
- **Product variability across studies.** Different trials have used different cell sources, doses, infusion schedules, and concurrent medications, making direct cross-trial comparisons challenging.
- **Mechanism in humans is not fully established.** While preclinical data strongly support immunomodulatory and paracrine mechanisms, the precise biological pathways operating in treated human patients are not yet fully characterized.

Research is ongoing, and the field is advancing rapidly. Larger, confirmatory trials are needed — and are being conducted — to build on the promising signals seen to date.

5. Safety Profile: What the Research Shows

An Honest Assessment

Understanding the safety of any medical intervention is as important as understanding its potential benefits. Based on the published clinical literature, hUC-MSC therapy for Type 2 diabetes has demonstrated a **favorable short-term safety profile** in the trials conducted to date. However, it is equally important to acknowledge the limitations of what we currently know.

Serious Adverse Events

Across the randomized clinical trials and pilot studies of UC-MSC therapy in adults with Type 2 diabetes, **no treatment-related serious adverse events (SAEs) have been reported** in the published trial literature [15, 16, 22]. This includes the Phase II randomized, double-blind, placebo-controlled trials by Zang et al. (2022 and 2023), as well as the safety evaluation published by Lian et al. in *World Journal of Clinical Cases* (2023), which was specifically designed to assess the safety of repeated intravenous UC-MSC infusions in T2DM patients [22].

The absence of treatment-related SAEs across multiple independently conducted studies is an encouraging signal, though it must be interpreted in the context of the relatively modest sample sizes and limited follow-up durations of these trials.

Tolerability and Mild Effects

Clinical trial reports consistently describe intravenous UC-MSC administration as **generally well tolerated** in people with Type 2 diabetes [15, 16, 22]. The Phase I/II diabetic foot ulcer study using hUC-MSC-derived secretome also reported the intervention as well tolerated with no significant adverse events in that small cohort [20].

It is important to note that published trial reports do not consistently provide detailed, quantified rates of specific mild adverse effects (such as transient fever, chills, or infusion reactions). This reflects a limitation in the granularity of reporting across the published literature, not necessarily an absence of any mild effects. Patients should discuss potential side effects with the Auragens medical team before treatment.

Delivery Route and Monitoring

Intravenous infusion is the most commonly used delivery route in the randomized clinical trials for T2DM, and it has been demonstrated to be feasible and tolerated in clinical settings [15, 16]. Preclinical research has explored alternative delivery routes (including intramuscular injection) and found that route of administration can affect cell distribution and biodistribution profiles — an area of ongoing investigation that may inform future clinical protocols [12].

For complications-focused applications, local or perilesional delivery has also been reported to be well tolerated in small studies [19, 20].

Standard clinical monitoring during and after intravenous infusion is part of the Auragens treatment protocol, consistent with the oversight applied in published clinical trials.

What We Still Need to Learn

The current safety evidence has meaningful limitations that must be acknowledged:

- **Long-term safety data are limited.** Most trials have follow-up periods of weeks to months. The long-term risk profile of repeated hUC-MSC infusions — including rare or delayed adverse events — has not been fully characterized in the available literature.
- **Sample sizes are modest.** Rare adverse events, by definition, require large populations to detect reliably. The current evidence base, while encouraging, cannot rule out the possibility of rare risks.
- **Route-specific and dose-specific risks.** The safety of different dosing regimens and administration routes requires further study.

Auragens is committed to transparency about what the science shows — and what it does not yet show. The favorable short-term safety profile seen in clinical trials is meaningful, but it does not substitute for the larger, longer-term studies that the field needs to fully characterize the risk profile of this therapy.

6. What to Expect Next at Auragens

Your Consultation

If you are considering hUC-MSC therapy for Type 2 diabetes, your journey at Auragens begins with a comprehensive medical consultation. This is not a sales conversation — it is a thorough, evidence-based medical review designed to determine whether this investigational therapy may be appropriate for your specific situation.

During your consultation, the Auragens medical team will:

- **Review your complete medical history**, including your diabetes history, duration of diagnosis, current medications, HbA1c and glucose monitoring data, and any diabetes-related complications
- **Discuss your treatment goals** — whether you are focused on improving blood sugar control, reducing insulin requirements, protecting against complications, or a combination of these objectives
- **Assess your residual beta cell function**, including available C-peptide data, which research suggests is an important predictor of response to UC-MSC therapy
- **Review the current evidence** with you honestly, including what the clinical trials show, what they do not show, and where the uncertainties lie
- **Discuss realistic expectations** — neither overstating what this therapy may offer nor dismissing the promising signals that have emerged from clinical research
- **Explain the treatment process** in detail, including the number of infusions, the schedule, what to expect during and after treatment, and the monitoring plan

Personalized Planning

Every patient's situation is different. The Auragens team will work with you to develop a personalized treatment plan that takes into account your medical history, current health status, treatment goals, and the current state of the evidence. We will coordinate with your existing diabetes care team to ensure continuity and safety.

Transparency and Communication

At Auragens, we believe that informed patients make better decisions. We will never pressure you toward a decision, and we will never overstate what this therapy can offer. Our commitment is to give you the most accurate, up-to-date, and honest picture of where the science stands — so that you can make a decision that is right for you.

7. Next Steps

Who May Want to Explore a Consultation?

This guide is designed for patients who are curious about whether hUC-MSC therapy may be relevant to their situation. You may want to explore a consultation if:

- You have been living with Type 2 diabetes for some time and are finding it increasingly difficult to achieve your blood sugar goals despite current medications
- You are on insulin therapy and are interested in exploring whether a regenerative approach might support a reduction in your insulin requirements over time
- You still have measurable residual beta cell function (C-peptide levels) and are interested in whether therapy might help preserve that function
- You are experiencing diabetes-related complications — such as peripheral neuropathy, kidney disease, or foot problems — and are interested in whether regenerative approaches may complement your existing care
- You are simply curious and want to have an informed, evidence-based conversation about your options

Questions to Consider Before Your Consultation

Coming to your consultation prepared will help you get the most out of the conversation. Consider reflecting on the following questions:

- What are my primary goals for my diabetes management? (Better blood sugar control? Reduced insulin dependence? Complication prevention?)
- What is my most recent HbA1c, and how has it changed over the past few years?
- Do I have recent C-peptide test results?
- What medications am I currently taking, and how well are they working?
- What complications, if any, have I developed?
- What does my current diabetes specialist think about regenerative approaches?

The Importance of Your Existing Care Team

hUC-MSC therapy is investigational, and it is not a replacement for your current diabetes care. We strongly encourage you to discuss your interest in this therapy with your endocrinologist, primary care physician, or diabetes specialist. The Auragens team is happy to communicate with your existing providers to ensure coordinated, safe, and well-informed care.

A Message of Hope

Living with Type 2 diabetes means navigating a condition that, for now, medicine cannot fully resolve. It means daily decisions, ongoing monitoring, and the awareness that the disease can progress even when you are doing everything right. That reality deserves to be acknowledged — not minimized.

At the same time, the science of regenerative medicine is advancing in ways that would have seemed remarkable just a decade ago. The research on hUC-MSC therapy for Type 2 diabetes — while still early — has produced genuinely encouraging findings: meaningful improvements in blood sugar control, more time spent in healthy glucose ranges, reductions in insulin requirements for many patients, and a safety profile that, in the studies conducted so far, has been favorable.

We do not know yet whether this therapy will fulfill its early promise at a larger scale. We do not know which patients will respond most strongly, or how long the benefits may last, or what the optimal treatment protocol looks like. These are honest uncertainties, and they are the reason that research continues.

What we do know is that the biological mechanisms that hUC-MSCs act upon — chronic inflammation, beta cell stress, insulin resistance, oxidative damage — are real, well-characterized contributors to the progression of Type 2 diabetes. The idea that addressing these root causes through regenerative medicine could complement and extend the benefits of current therapy is scientifically grounded, not speculative.

Hope, in medicine, is most valuable when it is honest. We hope that this therapy proves to be a meaningful addition to the options available to people living with Type 2 diabetes. We are committed to pursuing that possibility with rigor, transparency, and deep respect for the patients who trust us with their care.

If you are ready to learn more, we invite you to reach out to the Auragens team. We are here to help you understand your options — and to walk alongside you on this journey.

The Auragens Patient Care Team

References

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