ARCH
Annual Review of Changes in Healthcare

A Guide to Mounjaro for the Treatment of Type 2 Diabetes Mellitus

Paige Willms, PharmD Candidate 2025[1]
[1]University of Findlay College of Pharmacy

Abstract

Type 2 diabetes mellitus is the most common type of diabetes. There are currently a variety of medications available for the treatment of the disease state. Mounjaro (tirzepatide) is an innovative medication that is the first in its class for the treatment of type 2 diabetes. Mounjaro is a once weekly injection that has been shown to improve outcomes of Type 2 diabetes. Mounjaro is a Glucagon-Like Peptide 1/Glucose-dependent insulinotropic polypeptide (GLP-1/GIP) co-agonist and has been shown to lower hemoglobin A1C in combination with diet and exercise. It has also been shown to cause weight loss in patients with type 2 diabetes.

University of Findlay
College of Pharmacy

Volume 7, Issue 1

Diabetes mellitus refers to a group of diseases that affect how the body uses blood sugar (glucose). Glucose is an important source of energy for the cells that make up the muscles and tissues.[1] The Center for Disease Control and Prevention (CDC) reports that more than 37 million US adults have diabetes and that it is the seventh leading cause of death in the United States.[2] There are three main types of diabetes: type 1, type 2, and gestational diabetes.[2]

Type 1 diabetes is caused by an autoimmune reaction leading to the destruction of pancreatic beta cells causing the body to stop producing insulin. This type of diabetes is less common and affects 5-10% of patients who are diagnosed with diabetes.[2] Type 1 diabetes can occur at any age, but usually occurs before the age of twenty.[3] Patients tend to experience a rapid onset of symptoms which could include polyuria, polydipsia, polyphagia, and ketones that are present in the urine at the time of diagnosis.[3] Patients also test positive for the presence of islet cell autoantibodies which are the cause of the beta cell destruction.[3]

Type 2 diabetes involves a combination of both insulin resistance and abnormal insulin secretion. Genetic predisposition and environmental factors also plays a role in increased risk of developing type 2 diabetes.[3] Sedentary lifestyle, obesity, and metabolic syndrome all increase the risk of developing type 2 diabetes significantly.[3] Type 2 diabetes is the most common form of diabetes, affecting about 90% percent of patients diagnosed with diabetes.[3] Most patients are diagnosed with type 2 diabetes after the age of thirty.[3]

Gestational diabetes can occur in pregnant women who do not have type 1 or type 2 diabetes.[2] During pregnancy it is important to screen for gestational diabetes especially if risk factors are present. Gestational diabetes occurs after the second trimester (26 weeks) and is usually resolved after birth. Gestational diabetes increases the baby's risk of health problems like obesity and increased risk of developing type 2 diabetes in the future.[2] Gestational diabetes also increases the mother's risk of developing type 2 diabetes.[2]

Although prediabetes is not considered a type of diabetes, it is still important to mention because it significantly increases the risk of developing diabetes. In the United States, 96 million adults -more than 1 in 3- have prediabetes.[2] Patients with prediabetes have higher than normal blood sugar levels, but do not meet the criteria for a diagnosis of type 2 diabetes. The high blood sugar levels increase the risk of developing type 2 diabetes, heart disease, and stroke.[2] Prediabetes is often reversible with diet and lifestyle changes.

The American Diabetes Association (ADA) 2023 guidelines- Standards of Care in Diabetes, outline the treatment pathways for type 2 diabetes. The treatment pathway varies depending on the patient's

comorbidities and therapy goals. The ADA provides specific recommendations for glycemic control and weight management.

For glycemic control, the ADA recommends an efficacy-based approach. The ADA lists dulaglutide (high dose), semaglutide, tirzepatide, and insulin with the combination of a GLP-1 receptor agonist as very high efficacy medications.[3] The next category is high efficacy medications, which includes GLP-1 receptor agonists (that were not listed in the very high efficacy level), metformin, SGLT2 inhibitors, sulfonylureas, and TZDs.[3] The last category is ranked as intermediate efficacy and includes DDP-4i.[3]

The ADA also recommends setting individualized weight loss goals. Lifestyle education involving medical nutrition, therapy/eating patterns, and physical activity, weight management programs, and the consideration of weight loss medication or metabolic surgery are all important to consider.[3] The ADA recommends considering a regimen with high-to-very-high dual glucose and weight efficacy theories.[3]

The newest medication, Mounjaro (tirzepatide), was approved in May 2022 and had recently been added to the ADA's guidelines for the treatment of type 2 diabetes. Tirzepatide is an injection that can be used to improve blood sugar and lower A1c when combined with diet and exercise.[4] Tirzepatide is the first diabetes medication to act as a GIP/GLP-1 Receptor co-agonist. Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are hormones involved in blood sugar control. Both hormones are released in the ileum, colon, and rectum.[3] They are also part of a class known as incretins. Once food has been ingested, the body begins secreting these hormones. GLP-1 then binds to receptors on the pancreatic alpha and beta cells. This binding triggers insulin secretion, suppresses glucagon secretion, increases satiety within the CNS, and slows the rate of gastric emptying.[3] The positive effects that are triggered by the release of incretins can be useful in the treatment of type 2 diabetes because incretins help to control a person's blood sugar. It has been shown that lowering a type 2 diabetic's A1c is associated with a lower risk of developing complications.[3] Since tirzepatide is a co-agonist, is helps to increase the levels of both GLP-1 and GIP.[3]

Three different doses of tirzepatide (5mg, 10mg, and 15mg) were evaluated in five clinical trials as either a stand-alone therapy or as an add-on to other diabetes medications.[4] The trials were combined in a Phase III SURPASS program and the trials were named, SURPASS-1, SURPASS-2, SURPASS-3, SURPASS-4, and SURPASS-5.[5] In SURPASS-2, SURPASS-3 and SURPASS-4, tirzepatide was studied as an add-on to the common diabetes medications metformin, sulfonylureas, and/or sodium-glucose co-transporter 2 inhibitors (SGLT-2 inhibitors).[5] For SURPASS-5, Mounjaro was evaluated in combination with basal insulin with or without metformin.[5]

The efficacy of Mounjaro was compared to placebo, a GLP-1 receptor agonist (semaglutide) and two long-acting insulin analogs.[4] Patients were randomized to receive the maximum recommended dose of Mounjaro (15 mg) and had a lowering of their hemoglobin A1c (HbA1c) level by 1.6% more than the placebo when used as a stand-alone therapy, and 1.5% more than the placebo when used in combination with a long-acting insulin.[4] In trials comparing Mounjaro to other diabetes medications, patients who received the maximum recommended dose of Mounjaro had lowering of their HbA1c by 0.5% more than semaglutide, 0.9% more than insulin deglutec, and 1.0% more than insulin glargine.[4]

In the 40-week SURPASS trials, patients taking tirzepatide had, their A1c lower on average by 2.0% on the 5 mg dose, 2.2% on the 10mg dose, and 2.3% on the 15 mg dose.[6] The patients taking semaglutide only saw a reduction in A1c of approximately 1.9%.[6] Eighty two percent of patients taking tirzepatide 5mg dose achieved an A1c below 7% on the 5 mg dose, 86% reached an A1c under 7% on the 10 mg dose. Eighty six percent of patients achieved an A1c below 7% on the 15 mg dose. [6] For the patients taking semaglutide, 79% achieved an A1c under 7%.[6]

Tirzepatide was also found to lead to significantly greater weight loss in patients compared to the other medications.[5] Patients treated with 5 mg of tirzepatide lost on average 12 lbs. and those given 15 mg lost an average of 25lbs.[5] Mounjaro is currently being studied for its weight loss potential.[5] There are other agents, i.e., Saxenda (liraglutide) and Wegovy (semaglutide), that are approved specifically for weight loss so it will be interesting to continue to follow these trial results for tirzepatide.

Tirzepatide can be administered at any time of day, and it is given once weekly.[6] Tirzepatide should be administered on the same day every week, but if the dosing day needs to change then it is recommended that there is at least 3 days (72 hours) between doses. [6] If a dose is missed then the missed dose should be given as soon as possible within 4 days (96 hours) after the missed dose. [6] If more than 4 days have passed, then the missed dose should be skipped before returning to the regularly scheduled day.[6]

Tirzepatide is packaged in a single-dose pen that does not require mixing.[6] This design helps to ensure ease of use for patients to dose themselves at home rather than relying on a clinic.[6] Tirzepatide needs to be stored in the refrigerator and cannot be frozen. [6] Tirzepatide can be stored at room temperature but will only last 21 days unrefrigerated. [6]

The most common side effects associated with tirzepatide are nausea, vomiting, and diarrhea.[6] To help decrease/lessen the nausea and vomiting, tirzepatide is started at a lower dose and then is titrated up as tolerated.[6] Eating smaller meals and avoiding fatty foods can help to limit these side effects.[6]

The less common, but more serious side effects associated with the use of tirzepatide include: pancreatitis, hypoglycemia, allergic reactions, kidney failure, sever stomach problems, changes in vision, and gallbladder problems.[6] Tirzepatide should not be used in patients that have a history or family history of any type of thyroid cancer, medullary thyroid carcinoma, or Multiple Endocrine Neoplasia syndrome type 2.[6] During the trials previously mentioned, it was found that tirzepatide could cause thyroid C-cell tumors in rats, and it is unknown if it could cause these tumors in humans.[4]

Tirzepatide is only available as a brand name drug and does not yet have a generic version available.[8] On average, tirzepatide costs over $300 per 0.5 mL of any strength.[8] Cost can be a factor to consider before a patient is started on the treatment of tirzepatide. Tirzepatide is also not indicated for the treatment of Type 1 diabetes or for the treatment of gestational diabetes.[8]

Trizepatide is an innovative new drug that has promising potential. It will be interesting to see how the medication compares over time and the creation of new competitive drugs it will lead to.

References:

1. Diabetes [Internet]. Mayo Clinic. Mayo Foundation for Medical Education and Research; 2022 [cited 2023Jan16]. Available from: https://www.mayoclinic.org/diseases-conditions/diabetes/symptoms-causes/syc-20371444#:~:text=Diabetes%20mellitus%20refers%20to%20a,of%20diabetes%20varies%20by%20type.
2. What is diabetes? [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2022 [cited 2023Jan16]. Available from: https://www.cdc.gov/diabetes/basics/diabetes.html
3. Diabetes care [Internet]. American Diabetes Association. 2023 [cited 2023Feb2]. Available from: https://diabetesjournals.org/care/issue/46/Supplement_1
4. Commissioner Of the FDA approves novel, dual-targeted treatment for type 2 diabetes [Internet]. U.S. Food and Drug Administration. FDA; [cited 2023Jan16]. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-novel-dual-targeted-treatment-type-2-diabetes
5. Mounjaro (tirzepatide) for the treatment of type 2 diabetes, USA [Internet]. Clinical Trials Arena. 2023 [cited 2023Jan16]. Available from: https://www.clinicaltrialsarena.com/projects/mounjaro-tirzepatide-type-2-diabetes/#:~:text=Clinical%20trials%20on%20Mounjaro,was%20studied%20as%20a%20monotherapy.
6. What is Mounjaro for adults with type 2 diabetes: Mounjaro™ (tirzepatide) [Internet]. Mounjaro. [cited 2023Jan16]. Available from: https://www.mounjaro.com/what-is-mounjaro#about-mounjaro
7. The 9 notable side effects of tirzeptide (Mounjaro) [Internet]. GoodRx. GoodRx; [cited 2023Jan16]. Available from: https://www.goodrx.com/tirzepatide/common-side-effects
8. Mounjaro and cost: Reducing long-term drug costs and more [Internet]. Medical News Today. MediLexicon International; [cited 2023Jan16]. Available from: https://www.medicalnewstoday.com/articles/drugs-mounjaro-cost#brand-name-vs-generic