Review Article

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2023.52.008226

Managing Obesity with Mounjaro: A Brief Literature Review

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ARTICLE INFO

Received: August 08, 2023

Published: August 17, 2023

Citation: Radwa Clarissa Omar. Managing Obesity with Mounjaro: A Brief Literature Review. Biomed J Sci & Tech Res 52(2)-2023. BJSTR. MS.ID.008226.

ABSTRACT

Mounjaro (tirzepatide) is both a glucagon like peptide (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptor agonist that was developed for the treatment of Type 2 Diabetes Mellitus (T2DM). Mounjaro was approved in May 2022 by the United State Food and Drug Administration (USFDA) as the first and the only GLP-1 and GIP receptor agonist to treat T2D. Obesity and diabetes are becoming an increasing global problem, particularly in Western populations, referenced as the twin epidemics. Mounjaro, labeled a twincretin, is unique as the only GLP-1 and GIP receptor agonist, responsible for significant reduction in glycemic levels and improvement of insulin sensitivity, as well as reduction of total body weight by more than 20%. After its development by Eli Lilly in 2022, the start of a new era began of dual therapeutic options for the management of both T2DM and obesity. The objective of this article is to briefly review the literature concerning the weight loss implications of a new medication, Mounjaro, to educate primary care clinicians concerning the potential for weight management in patients without T2DM, who are overweight and/or obese.

Keywords: Mounjaro; Obesity; Weight Loss; Tirzepatide; Weight Reduction; Metabolic Syndrome; Clinical Trials

Abbreviations: GLP-1: Glucagon Like Peptide; T2DM: Type 2 Diabetes Mellitus; USFDA: United State Food and Drug Administration; GIP: Glucose-Dependent Insulinotropic Polypeptide; FDA: Food and Drug Administration; NASH: Non-Alcoholic Steatohepatitis

Introduction

Obesity is a metabolic disease, linked to numerous chronic diseases, with recent statistics suggesting that being overweight/obese is consuming the global population. It is approximated that approximately 30% of the global population are overweight. Mounjaro is the first dual GLP-1 and GIP agonist for the treatment of T2DM, obesity and steatohepatitis (Lin, et al. [1]), and was FDA approved in May 2022 to achieve glycemic control in adults with T2DM, in addition to dietary modification and exercise. Mounjaro has been shown to lower hemoglobin A1C even more than other medications similar to its class. Additionally, there is evidence present that Mounjaro plays a critical role in the weight loss of patients with T2DM, and does not increase the risk of major cardiovascular events. Mounjaro supported significant weight loss in recent clinical trials, supporting the potential for its use in the management of obesity.

Google Scholar was utilized to search keywords, "Mounjaro", "Obesity", "Weight Loss", "Tirzepatide", "Weight Reduction", "Metabolic Syndrome" and "Clinical Trials" for this literature review. The literature search was last performed on 1st August 2023 and was limited to English manuscripts published anytime from 2022 to present. Of importance to note, current published data on the correlation between obesity management and Mounjaro, include literature reviews, meta-analyses, case reports, and systematic reviews.

Weight Loss Implications of Mounjaro (Tirzepatide)

Tirzepatide has been shown to produce a marked decrease in glucose levels, both fasting and postprandial, while also promoting decline in food consumption and body weight in persons with Type 2 Diabetes. Following 28 weeks of treatment with tirzepatide in one study, of note was marked improvement of insulin sensitivity in those

with hyperinsulinemia. In the same study, tiraepatide lowered fasting glucagon levels by 28%, compared to no difference at all with the placebo. Tirzepatide delays gastric emptying and subsequently reduces postprandial hyperglycemia by slowing glucose absorption (Ali, et al. [2]).

One study reports that Tirzepatide has yielded promising results in terms of body weight reduction, according to human clinical trials comparing similar medications including semaglutide and dulaglutide. The USFDA has approved tirzepatide for the management and treatment of Type 2 Diabetes, but it has proven to be a revolutionary agent for achieving weight loss, as well. Additionally, patient compliance appears to be favored, as tirzepatide is offered as a once weekly injection (Chavda, et al. [3]).

In May 2022, the FDA granted approval for the use of tirzepatide in the management of obesity. It is a first of its kind medication activating two separate receptor sites, causing greater satiety and lessened food intake. The SURMOUNT-1 trial provided comparison of weekly escalating doses of tirzepatide with placebo in over 2500 adults without Type 2 Diabetes with an average age of 45, BMI of 38 and eGFR of 98. By week 72, participants had lost 14% total body weight on only 5mg weekly tirzepatide and 20% at 15mg. Of note, 78% of individuals on 15mg lost ≥15% of baseline weight, 63% lost ≥20% of baseline weight, and 40% lost ≥25% of baseline weight (Friedman, et al. [4]).

Tirzepatide (Mounjaro) is the only dual receptor agonist on the market marked a "twincretin" due to its mimicking of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). Originally used to treat T2DM, tirzepatide has been shown markedly effective in the treatment of obesity. According to one recent study, 85% of participants on the 5mg dose, 89% on 10mg and 91% on 15mg showed marked reduction in body weight opening a pathway of tirzepatide as an antiobesity drug. When comparing efficacy of tirzepatide to semaglutide in the SURPASS-2 clinical trials tirzepatide was proven to reduce body weight and A1C levels more effectively than semaglutide proving it to be a powerhouse in the management of obesity and Type 2 Diabetes. Another trial depicting tirzepatide efficacy exhibited up to a 22.5% weight reduction in obese adults (Siddiqui, et al. [5]).

Three separate dosages of tirzepatide (5, 10, and 15 mg) were evaluated in 5 clinical trials as either independent treatments or as adjunct treatment to existing diabetic regimens, and The efficacy of Tirzepatide was compared to a placebo, a GLP-1 receptor agonist, and two long-acting insulin analogs. participants in the clinical trials had an average BMI of 32–34 kg/height in m2 and experienced an average weight reduction of 15 pounds greater with tirzepatide compared to placebo without additional insulin and 23 pounds greater than placebo when both were taken concurrently with insulin. Participants lost 12 more pounds on tirzepatide compared to semaglutide, 29 more pounds in comparison to insulin degludec, and 27 more pounds compared to insulin glargine (Dhirani, et al. [6]).

In the SURMOUNT-1 pivotol trial evaluating the effects of tirzepatid, the percentage weight loss evaluated yielded the most noteable seen in any anti-obesity, weight loss trial to date, compared to that observed prior with semaglutide in the STEP-2 trial. The SURMOUNT-2 trial of tirzepatide held its primary focus on patients with T2D who were also overweight/obese, and reported that after 72 weeks on high doses of tirzepatide, a safe reduction of 12.8%-14.7% in body weight was noted. This finding was suggested to likely lead to US Food and Drug Administration (FDA) approval of a weight loss indication for tirzepatide in the near future (Idris, et al. [7]).

The effect of tirzepatide on body weight could make it very useful as a weight loss medication. Based on one study, tirzepatide was noted to be more effective than other medications in reducing body weight. According to Lin (2023), "most drugs currently used to treat obesity started out as treatments for diabetes". Weight loss effects were compared between tirzepatide and placebo, insulin and GLP-1 medications, with results indicating that tirzepatide could reduce weight in T2DM patient who are also overweight. It was also shown that compared with medications like liraglutide and semaglutide, tirzepatide produced better weight loss outcomes in non-diabetic patients (Lin, et al. [1]).

Tirzepatide is currently approved for the treatment and management of Type 2 Diabetes, but has also been fast-tracked for the treatment of obesity by the manufacturing company, and judging by clinical results, tirzepatide has been implied as "one of the most effective obesity drugs yet." Nearly two thirds of obese patients without T2DM achieved at least a 20% reduction in weight in the phase 3 SURMOUNT-1 trial, noted to be even more effective than the popular drug, Wegovy (semaglutide). Tirzepatide, while appearing useful in the management of both T2DM and obesity, is also in development for non-alcoholic steatohepatitis (NASH), heart failure and obstructive sleep apnea (Senior [8]).

Conclusion

The early clinical development of a ground breaking medication, such as Mounjaro, with the capability of marked decreases in glucose levels, increased insulin sensitivity, reduction in weight, and management of dyslipidemia has been crucial. Consequently, Mounjaro appears to be both a highly effective antidiabetic drug, as well as an effective obesity treatment. (Dhirani, et al. [6]). The therapeutic efficacy of Mounjaro is likely to alter the treatment structure for obesity and could prove to be a highly effective staple in treating obesity. Easy administration, once a week convenience, and the management of multiple diseases are just three reasons why Mounjaro is a promising medication in the long run (Siddiqui, et al. [5]).

Conflict of Interest Statement

The author declares that there is no conflict of interest.

Ethic Statement

This article does not contain any studies involving human participants performed by the author.

Funding

The author received no financial support for the research, authorship or publication of this article.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.52.008226

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Submission Link: https://biomedres.us/submit-manuscript.php