Comparative Review on Semaglutide vs. Trizepatide for the Treatment of Type 2 Diabetes

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder, which leads to elevated levels of blood sugar and is characterized by beta-cell malfunctioning and resistance to insulin. The pressure to find safer and more efficient treatment options has reached an urgent situation with a rapid growth of type 2 diabetes in the world population due to the failure of traditional antidiabetic drugs to manage weight and cardiovascular risk. The paper will review the pharmacological, clinical, safety, and efficacy of tirzepatide and semaglutide, novel incretin-based agents in the treatment of type 2 diabetes, and the cardiovascular benefits of semaglutide, which is a selective GLP-1 receptor agonist and to significantly improve glycemic control (reducing HbA1c by 1-1.8) and induce a 4-5 kg weight loss. Both medications have similar adverse effects on the gastrointestinal system, resulting in weight loss of 7-12 kg and reduction of HbA1c by 2.0-2.4, with both drugs experiencing similar side effects, such as nausea and vomiting, which are mostly moderate and dose-dependent. Emerging data also suggest other benefits, including, but not limited to, improved hepatic steatosis with semaglutide and potential cardiovascular advantages with tirzepatide, which translate to the fact that these two drugs offer weight loss and glycemic control with high tolerance. Semaglutide has the advantage of oral administration and demonstrated cardiovascular safety whereas tirzepatide demonstrates slightly improved metabolic outcomes. To patients with type 2 diabetes mellitus, the drugs represent the dawn of a new age of personalized and comprehensive metabolic treatment.

Keywords: *Type 2 diabetes mellitus, Semaglutide, Tirzepatide, GLP-1 receptor agonist, GIP agonist, Glycemic control, Weight loss, Incretin therapy.*

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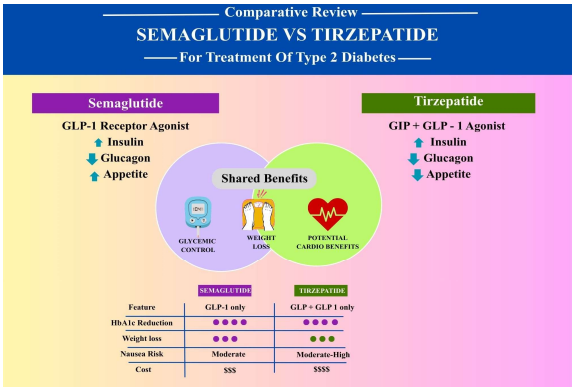
GRAPHICAL ABSTRACT



1. INTRODUCTION

1.1 Background of Type 2 Diabetes

Diabetes mellitus type 2 (T2DM) is a chronic metabolic condition caused by a lack of insulin production and resistance to "insulin which decreases the uptake of glucose in fat, muscle, and liver cells, which is an early sign of this condition and is increasing in prevalence in the population worldwide, with distinct differences depending on age, and ethnicity[1,2]. As an example, 2001-2009 reported a rise in prevalence in most of the racial groups but some of them such as the Asian Pacific Islanders did not show significant changes[3]. T2DM develops as a result of genetic, environmental and lifestyle factors. The aim of the management is to stabilize the condition of the blood sugar level, avoid complications, and improve the metabolic condition[4]. The stabilization of the level of blood sugar, the prevention of complications, and the improvement of the overall metabolic health are the objectives of the management[5]. The first one is lifestyle changes, such as healthy eating, exercise and weight loss[6]. In case of the inadequacy of lifestyle changes, medication is required[7]. Metformin is the usual initial treatment option, as it reduces the liver production of glucose and increases the insulin sensitivity, although it does not improve the resistance to insulin or the insulin production of the beta-cells, exposing the patients to the risk of long-term complications[6,8]. Other common medications are also used successfully in lowering the blood sugar level, however, they do not improve the insulin insensitivity or insulin production of the beta-cells in the liver, which also leaves the patients susceptible to the adverse effects of the conditions over time. GLP-1 receptor agonists, which include semaglutide, and dual GIP/GLP-1 receptor agonist which include tirzepatide are able to stimulate glucose-dependent insulin secretion, reduce glucagon secretion, delay gastric emptying, and enhance satiety. These treatments are not only beneficial in terms of glycemic control and weight loss, but also provide cardiovascular and renal outcomes, which have never been met in existing treatment methods, thus being a significant change in T2DM treatments[9,10].

1.2 Need for Improved and Targeted Therapies

The prevalence of type 2 diabetes mellitus (T2DM) is rising quickly and is a serious public health issue[6]. It is a rapidly growing disease which commonly requires multiple pharmacotherapy. Many oral antidiabetic drugs (OADs) are available for patients with type 2 diabetes mellitus (T2DM) [7]. However, it is acknowledged that more treatments are required, and a number of new substances are currently" in advanced phases of development. The available treatment methods may have little impact on the severity of the condition and have unfavourable adverse effects, especially weight gain and hypoglycemia, as well as contraindications. One of the more recent treatments for improving glycaemia is incretin-based therapy, which is available in two forms: glucagon-like peptide-1 (GLP-1) agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors.[8] When these drugs are used, insulin production increases "glucose-dependently" and glucagon decreases, improving glycaemia and decreasing the risk of hypoglycemia[8].

1.3 Advances in Incretin-Based Therapies in Type 2 Diabetes

Conventional treatments for hyperglycemia, which include insulin, sulfonylureas, and metformin, often fail to identify the underlying pathophysiological mechanismsAfter meals, the gut secretes incretin hormones, mainly GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic polypeptide)[11]. In addition to decreasing stomach emptying and inhibiting glucagon release, they also raise insulin release from pancreatic β-cells in a glucose-dependent way, which reduces the risk of hypoglycemia by producing insulin when blood sugar levels are high[9]. GLP-1 receptor agonists (GLP-1 RAs) and DPP-4 inhibitors are two examples of incretin-based therapies that have gained popularity for improving glycemic control, reducing body weight, and protecting the kidneys and heart.

Clinical Role –

- Suggested by the ADA/EASD recommendations as a second-line treatment after metformin.
- Preferred among patients suffering from kidney illness, cardiovascular disease, or obesity. Offer advantages over sulfonylureas and insulin in terms of reducing the risk of hypoglycemia and managing weight[12].

2. METHODOLOGY

This review was prepared by examining previously published studies that discussed the use of semaglutide and tirzepatide in the treatment of type 2 diabetes mellitus. Relevant literature was gathered from commonly used scientific sources, including PubMed, Google Scholar, Science Direct, Scopus, and ClinicalTrials.gov. Articles published between 2016 and 2025 were considered. Search terms related to the drugs and disease, such as semaglutide, tirzepatide, incretin-based therapy, GLP-1 receptor agonist, dual GIP/GLP-1 agonist, blood glucose control, weight reduction, and cardiovascular effects, were used in different combinations. Findings from well-known clinical trial programs (SUSTAIN, PIONEER, SURPASS, and SURMOUNT) were reviewed in detail because of their importance in clinical decision-making. Only studies that provided clinically meaningful information, including randomized trials, meta-analyses, and review articles involving adult

patients, were included. Reports with limited data, conference abstracts, non-English publications, and animal-only studies were not considered. The selected literature was examined qualitatively, and the information was summarized to compare the efficacy, safety, and metabolic outcomes of semaglutide and tirzepatide.

3. SEMA-GLUTIDE

3.1 Introduction

Semaglutide is an agonist of the glucagon-like peptide-1 (GLP-1) receptor (GLP-1RA) that resembles human GLP-1 by 94%[13]. It was the first GLP-1RA created with oral use in mind. In order to treat type 2 diabetes mellitus (T2DM), a novel family of drugs called glucagon-like peptide-1 receptor agonist (GLP-1 RAs) became accessible in 2005[14]. When diet and exercise alone are insufficient to achieve appropriate blood sugar management in type 2 diabetes, semaglutide can be used either alone, particularly for those who cannot tolerate metformin, or in combination with other glucose-lowering medications, such as insulin. Semaglutide has just been licensed by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) to treat type 2 diabetes (T2DM)[13].

3.2 Mechanism of action

The mechanism of action of semaglutide is represented in Fig. No. 1. Semaglutide works by activating the GLP-1 receptor and is structurally very similar to human GLP-1, with about 94% similarity[15]. Semaglutide lowers blood sugar and promotes weight reduction by activating GLP-1 receptors, which are mostly located in the brain, pancreas, and digestive tract. Semaglutide stimulates the release of insulin in response to elevated blood sugar levels following a meal when these receptors are active[16]. Simultaneously, it decreases glucagon release, slows stomach emptying, and promotes “the development of insulin-producing pancreatic cells. By doing this, hunger is lessened. Furthermore, semaglutide can reduce appetite, lessen the urge to eat, and increase feelings of satisfaction after eating when it interacts with GLP-1 receptors in the hypothalamus[17]. These various effects contribute to semaglutide's overall impact on managing blood sugar and supporting weight loss. Along with extended-release exenatide and dulaglutide, semaglutide is considered a long-acting GLP-1 receptor agonist[12].

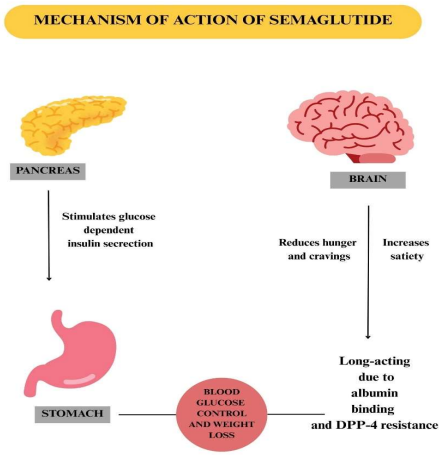


Fig. No. 1 Mechanism of action of semaglutide

3.3 Pharmacokinetics and dosing

Oral and subcutaneous semaglutide is a long-acting agonist of the glucagon-like peptide-1 (GLP-1) receptor[11]. Its pharmacokinetic properties are characterized by slow absorption, strong plasma protein binding, and an extended half-life of almost seven days, which together enable convenient once-weekly injection or once-daily oral dosing[18].

1. Absorption

On the one hand, semaglutide is a slowly absorbed drug in subcutaneous dosage with a peak plasma concentration 24-36 hours after administration[19]. The bioavailability of the injectable form is high (approximately 89%), and on the other hand, the oral formulation must address the endemic issues of peptide drugs, which include poor intestinal permeability and breakage in the stomach[20]. To avert this, semaglutide is combined with the absorption enhancer sodium N-(8[2-hydroxybenzoyl] amino) caprylate (SNAC). SNAC facilitates transcellular absorption across the stomach liner and elevates the local pH of the stomach[21].

2. Distribution

Once absorbed, semaglutide is bound firmly to plasma albumin (>99%)[22]. This high-affinity protein binding helps the molecule to remain in circulation and avoids the rapid disposal of the molecule. Consequently, semaglutide is retained in the vascular space to a large extent and has a relatively low volume of dispersion[23].

3. Metabolism and Elimination

Semaglutide cannot be cleared by single organ[18]. The peptide backbone undergoes the process of proteolytic cleavage and the fatty acid side chain is 2-oxidized in different organs. The resultant metabolites are excreted via urine and faeces[24]. Notably, unchanged semaglutide is hardly ever found in urine highlighting the significance of metabolic breakdown over direct renal clearance[25].

4. Dosing and Half-Life Implication.

One of the identifying properties of Semaglutide is its half-life that is long (between 145 and 184 hours or between one and a week). Interestingly, the half-life of oral semaglutide does not change greatly following absorption, as such, the difference between daily and every-week doses is determined by drug absorption efficiency and not drug clearance. Empirical findings in four-five weeks of

consistent treatment normally yield steady-state levels[26].

3.4 Dosing Strategies for Semaglutide in Type 2 Diabetes

Semaglutide is among the most effective glucagon-like peptide-1 receptor agonist (GLP-1RAs) for enhancing glycemic control in type 2 diabetes. Both once-weekly subcutaneous injections and once-daily oral tablets have been made possible by its pharmacokinetic properties, particularly its prolonged half-life of around a week. Dosage regimes for the treatment of diabetes are carefully planned to maximize efficacy while maintaining gastrointestinal tolerability[27].

1. Subcutaneous Semaglutide: For the first four weeks, subcutaneous semaglutide is started in individuals with type 2 diabetes at a modest dose of 0.25 mg once weekly[28]. This initial dosage is meant to be a tolerance step that gives the gastrointestinal tract time to adjust, rather than to achieve glycaemic control. Following this time period, the dose is increased to the initial therapeutic level of 0.5 mg once weekly[18]. The dosage may be raised to 1.0 mg per week if better glycaemic control is required. Higher dosages of up to 2.0 mg per week are accessible in some areas and offer extra effectiveness in lowering glycated haemoglobin (HbA1c) and promoting weight loss[29]. Semaglutide's terminal half-life of 145–184 hours provide pharmacological rationale for the once-weekly dosage, ensuring steady plasma levels with few variations. Crucially, pharmacokinetic studies and clinical trials verify that absorption is the same whether injections are given in the upper arm, thigh, or abdomen, providing patients administration alternatives[30].

2. Oral Semaglutide: Patients with type 2 diabetes now have a non-injectable option thanks to the oral formulation. For 30 days, 3 mg once daily is the starting dosage[31]. Similar to the initial SC dose, this period helps reduce gastrointestinal side effects but does not result in a significant glycaemic improvement. The dosage is raised to 7 mg per day after 30 days. The dosage may be increased to a maximum of 14 mg once daily for people who need further glycaemic control.[31] Since oral semaglutide has a low bioavailability, it must be taken while fasting, with at least 120 millilitres of plain water, and 30 minutes or more prior to eating, drinking, or taking other medications. In accordance with these guidelines significantly decreases drug absorption and could affect effectiveness[32].

Dosing in Special Populations:

- Pharmacokinetics are not affected by kidney function, including patients with end-stage renal disease on hemodialysis; no dosage adjustments are required[33].
- For liver impairment, the drug exposure remains similar across mild, moderate, and severe cases; no dosage changes are needed.[32]
- In older adults or individuals with different body weights, those with higher body weights experience lower drug exposure, although official dosage modifications are not recommended.

3.5 Clinical Efficacy of Semaglutide in Glycemic Control:

Semaglutide has consistently demonstrated notable advantages in improving blood sugar (glycaemic) control in those with type 2 diabetes. The injected (subcutaneous) and oral formulations both promote weight loss and have a little risk of hypoglycemia., and reduce HbA1c by approximately 1–1.8%. Large clinical trial programs (SUSTAIN and PIONEER), meta-analyses, and experimental studies provide the evidence.

1. Subcutaneous Semaglutide (SUSTAIN program):

The effectiveness of once-weekly subcutaneous semaglutide was demonstrated by the SUSTAIN trials. Semaglutide decreased HbA1c by 1.5–1.8% over 30–56 weeks, more than sitagliptin, exenatide ER, dulaglutide, canagliflozin, or insulin did in several studies[34]. These results have been confirmed by a meta-analysis of 24 randomised controlled studies with more than 22,000 patients. When compared to a placebo, weekly HbA1c reductions were -1.14% with 0.5 mg and -1.37% with 1.0 mg. And still, semaglutide demonstrated greater reductions of 0.7–0.9% when compared to another antidiabetic medications[35].

2. Oral Semaglutide (PIONEER program):

Daily oral semaglutide is also very successful at controlling blood sugar levels, as demonstrated by the PIONEER studies. Oral semaglutide administered to insulin (± metformin) produced dose-dependent reductions in the PIONEER 8 study; at 52 weeks, up to 54% of patients had a HbA1c <7% without seeing an increase in hypoglycemia[36]. Oral semaglutide significantly lowered HbA1c, according to a recent meta-analysis of 9,541 patients:

- −0.61% with 3 mg
- −1.12% with 7 mg
- −1.08% with 14 mg vs placebo.
- Semaglutide produced reductions that ranged from 0.3% to 0.4% higher than those of the active drugs sitagliptin and empagliflozin. In everyday use, oral semaglutide has also demonstrated long-term advantages. In addition to modest weight loss, a multicenter trial indicated that 42% of patients achieved HbA1c <7% and HbA1c decreases of ~0.9% over 18 months[37].

3.6 Safety profile and side effects

The majority of adverse reactions associated with semaglutide are gastrointestinal (GI) and dose-

dependent, according to randomised studies and extensive meta-analyses. Notable indicators include a class-level rise in gallbladder/biliary illness with GLP-1 receptor agonists and diabetic retinal issues in patients with pre-existing retinopathy (particularly with rapid A1c decreases). Serious risks are rare. Overall, aggregate analyses do not show an elevated risk of pancreatitis[38].

Common (usually mild and related to dosage)

GI Side Effects: Discomfort in the abdomen, constipation, diarrhoea, vomiting, and appetite suppression. Mostly occur during dose increase or commencement; usually go away with time. Source: Safety review—increased risk of gallbladder and mild to moderate gastrointestinal disruption[39].

Important (less frequent but clinically significant)

and diabetic retinal issues in patients with pre-existing retinopathy (particularly with rapid A1c decreases). Serious risks are rare. Overall, aggregate analyses do not show an elevated risk of pancreatitis[38].

1. Cholelithiasis/Biliary Disease: GLP-1 RA users are at increased risk, particularly when using the drug for longer periods of time or at greater dosages[40]. Baseline retinal screening and monitoring is advised, particularly in high-risk situations; patients with pre-existing retinopathy and rapid A1c drop are at increased risk of deteriorating[39].

2. Acute Kidney Injury (AKI): There is a risk of dehydration due to gastrointestinal losses, such as diarrhoea or vomiting. Ensure adequate water intake during illness or when increasing the dose.

3. Thyroid C-cell Tumors: The medicine should not be used if there is a personal or family history of multiple endocrine neoplasia type 2 (MEN2) or medullary thyroid carcinoma (MTC), according to the boxed warning for thyroid C-cell tumors based on recent research. Keep an eye out for any voice changes or the existence of neck nodules[39].

4. Ocular Events (Rare): Non-arteritic anterior ischaemic optic neuropathy (NAION) reports: a potentially slight increase in risk. Promote the reporting of vision symptoms.

2.7 Impact of Semaglutide on Body Weight

A weekly dose of subcutaneous semaglutide reduces body weight by around 4-5 kg[40]. Taking 14 mg of semaglutide daily reduces weight by about 3 kg[41]. Compared to a placebo or other antidiabetic medications, a meta-analysis reveals noticeably more weight loss[42], reveal a weight decrease of approximately 10–12% (or 10–11 kg) compared to baseline. Actual data: Subcutaneous users: around 7.5% (about 17 pounds) lost. Oral users: after two years, ~4.4% loss (~9 lbs) [43].

4. TIRZEPATIDE

A new diabetic medication called tirzepatide has been approved by the Food and Drug Administration (FDA) [44]. It is the first of its kind to operate as a dual-acting agonist of the glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1) receptor[45]. It is approved for use as a dietary and exercise supplement to improve glycaemic control in people with type 2 diabetes mellitus (T2DM) in the USA, EU, Japan, and other countries. Tirzepatide's therapeutic efficacy is significantly greater than that of current drugs. A once-weekly subcutaneous injection used to control blood sugar in individuals with Type 2 diabetes was approved by the FDA in May 2022 under the brand name Mounjaro[46].

4.1 Mechanism of action

The mechanism of action of tirzepatide is represented in Fig. No. 2. The dual-agonist medication tirzepatide shows a clear preference for GIP receptors over GLP-1 receptors. Mechanistic studies have demonstrated that it has a stronger affinity for human GIP receptors than GLP-1 receptors,which results in a more efficent decrease of hyperglycemia than other GLP-1 receptor agonists and adds to its therapeutic efficacy[46]. His molecular design enables him to increase binding strenth between GIP and his GLP-1 sequence.[45] This imbalance nrrds to be maintained because:GIPR activation encourages the release of insulin from pancreatic.Beta cells which improves glycamic control[47]. High GLP-1R activity is often associated with dose- limiting gastrointestinal side effects , such as nausea and vomiting, which are reduced by decreased affinity for GLP-1R[29]. The pharmacokinetic properties of tirzepatide enable once-weekly dosing and continuous receptor stimulation because its C20 unsaturated di-acid acyl chain enables albumin binding[48].

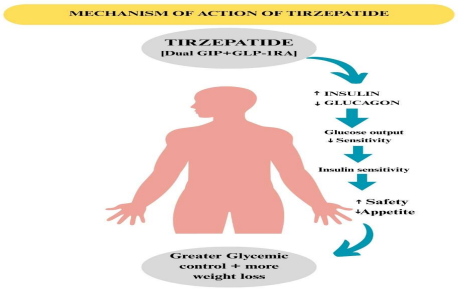


Fig. No. 2 Mechanism of action of tirzepatide

4.2 Pharmacokinetics

Absorption: The drug Tirzepatide needs to be injected under the skin through subcutaneous administration[48]. The drug reaches its peak blood concentration after 24 to 48 hours following its gradual absorption[49]. The amount of food consumed has no discernible impact on its absorption[48].

Distribution: The bloodstream system of Tirzepatide achieves approximately 99 percent plasma albumin binding once it enters the bloodstream.[48] The drug remains active for an extended period because its strong binding mechanism extends its time in the

bloodstream.[49] The drug exists as a moderate distribution volume because it maintains most of its presence in the bloodstream while spreading through different body fluids.[48]

Metabolism: Tirzepatide is a synthetic peptide that contains a chain of fatty acids[50]. The substance has minimal capacity to interact with other medications because liver enzymes especially CYP450 enzymes cannot break it down[51]. The body breaks down the substance through its natural process which uses proteolytic enzymes to convert it into smaller peptides and amino acids. The fatty acid component undergoes two chemical processes which are amide hydrolysis and β-oxidation[50]. The body eliminates the peptide medication through its standard protein degradation pathways instead of using liver and kidney functions[48]. The drug system shows slow clearance because its effects continue for an extended period[48]. The half-life duration lasts approximately five days which equals 120 hours[48]. The interval between doses should be set to one-week time periods[52].

Special Population

- Hepatic impairment (liver disease): Research indicates that exposure to tirzepatide does not significantly alter in mild, moderate, or severe liver disease, thus there is no need to modify the dosage[48].
- Renal impairment, or kidney disease: In a similar vein, renal issues have no discernible impact on PK[53].
- Body weight and age differences are negligible, therefore regular dosage is applicable.

4.3 Dosing

- **Route:** Subcutaneous (under the skin) injection.
- **Frequency:** Once weekly.
- **Dosing Schedule**: Start with 2.5 mg once weekly for four weeks to improve tolerance[29]. Escalation of dosage: Every four weeks, increase by 2.5 mg if tolerated[54].
- 5 mg, 7.5 mg, 10 mg, 12.5 mg, or up to 15 mg weekly maintenance dosages[55].
- A maximum dose of 15 mg is recommended once a week.

Special population

- Hepatic impairment: PK is unaffected and no dose modification is required[54].
- Elderly patients: No particular adjustments are required[55].

4.4 Clinical Efficacy of Tirzepatide in Glycemic Control

Numerous SURPASS clinical trials have evaluated tirzepatide in individuals with type 2 diabetes. Its ability to reduce HbA1c (average blood sugar over three months) was the primary objective. In people with type 2 diabetes, tirzepatide is a very good blood sugar regulator[56]. It helps most patients reach safe HbA1c levels, has a lower risk of hypoglycemia than insulin, and has been shown in numerous studies to perform better than semaglutide and insulin. Tirzepatide regularly reduces HbA1c by roughly 1.9–2.4% across studies, which is more effective than the majority of currently prescribed medications[57].

4.5 Safety Profile & Side Effects of Tirzepatide

General Safety

- In clinical trials, tirzepatide was generally well tolerated[58].
- The majority of side effects were minor to severe and mostly occurred when the dosage was increased or started[58].
- Serious adverse effects, such as extreme hypoglycemia, were uncommon, particularly when compared to insulin[59].

Common Side Effects (seen in many patients)

- Nausea (feeling sick)
- Diarrhoea
- Vomiting
- Decreased appetite
- Constipation[60].

Less Frequent Adverse Events

- Injection site reactions (redness, itching, swelling)
- Mild hypoglycemia (low blood sugar)– more likely if taken with insulin or sulfonylureas
- Indigestion, burping, or bloating.

Rare but Important Concerns

- Pancreatitis, or inflammation of the pancreas, is extremely uncommon but has been documented with GLP-1/GIP medications.
- Gallbladder problems, such as inflammation and gallstones.
- Potential risk for thyroid C-cell tumors (not demonstrated in humans, but seen in animal studies); however, avoidance is usually advised for people with a personal or family history of medullary thyroid cancer[45].

4.6 Effects of Tirzepatide on Body Weight

In addition to lowering blood sugar, tirzepatide also significantly reduces body weight, more so than the majority of diabetic medications, such as insulin and even semaglutide[21]. Significant weight reduction is consistently achieved with tirzepatide; among diabetics, this weight loss is frequently 7–12 kg. The more weight lost, the higher the dosage (15 mg) [61]. Tirzepatide aids in weight loss while enhancing blood sugar regulation, in contrast to insulin, which typically results in weight gain.

4.7 Safety profile and common side effects of tirzepatide

- In general, tirzepatide is easily tolerated; the majority of side effects are minor to severe and start early in the dose escalation process[29].
- Gastrointestinal problems represent the most common side effects which occur during treatment. The most common adverse effects, which typically begin during dose-up and gradually subside, include nausea, vomiting, diarrhoea, constipation, and decreased appetite[62].
- Moderate hypoglycemia risk: The risk of hypoglycemia is modest when tirzepatide is taken alone but it rises when combined with insulin or sulfonylureas[29].
- Pancreatitis: Doctors should keep track of pancreatitis through their methods because the disease shows no difference between patients and those who receive standard treatment according to pooled and meta-analytic studies" of acute pancreatitis cases[63].
- Gallbladder/biliary events: Reviews and clinical trials show that tirzepatide maximize the risk of gallbladder/biliary problems (such as cholelithiasis and cholecystitis) compared to controls; if patients experience biliary-type discomfort, this signal requires clinical attention[64].
- **Longer-term and real-world data:** New real-world research mostly supports trial safety signals (mostly GI adverse events and biliary events), but it also keeps an eye out for less common issues as usage grows.

5. Comparative analysis of Semaglutide and Tirzepatide

The comparative analysis of Semaglutide and Tirzepatide have been summarised in Table 1.

Table 1. Comparative analysis of Semaglutide and Tirzepatide

Outcomes	Semaglutide	Tirzepatide
Weight-loss results	Semaglutide 2.4 mg resulted in a mean weight decrease of 10–15% at 68–72 weeks in obesity trials (STEP).	Tirzepatide (5/10/15 mg) provided approximately 15–21% mean weight loss at 72 weeks in obesity studies (SURMOUNT-1), and in head-to-head longer-term assessments, it surpassed semaglutide[62].
Glycemic control (HbA_{1c})	In SUSTAIN/PIONEER programs, it lowers HbA_{1c} by approximately 1.5% to 1.9% (a high proportion attain <7%)[65].	Reduces HbA_{1c} ≈ −2.0 to −2.5% in SURPASS trials; superior to semaglutide in head-to-head (SURPASS-2 / other SURPASS studies) [29].
Cardiovascular outcomes	Semaglutide has demonstrated reduction in major adverse CV events (MACE) in dedicated CVOTs (SUSTAIN-6 and SELECT show significant benefit)[65].	The definitive large dedicated CVOT data are still emerging, although tirzepatide pooled analyses/meta-analysis indicate no increased CV risk and a tendency towards decreased MACE (pre-specified SURPASS meta-analysis) [66].
Patient adherence & discontinuation	Weekly injection; trials show nontrivial discontinuation (~10–15%) often related to GI AEs, cost, or access; real-world persistence varies by healthcare setting.	Weekly injection is also common; trial discontinuation is often between 7 to 12% (GI and dose-titration issues are significant); some head-to-head data show similar or

		marginally lower discontinuation compared to semaglutide[29].
Safety & tolerability	GI (nausea, vomiting, diarrhoea) adverse events are common; semaglutide trials reveal nausea of approximately 15–20% along with dose-dependent early adverse events and class signs[67].	Similar GI adverse-event profile (often dose-dependent); some trials report somewhat higher GI event rates at the highest tirzepatide doses versus semaglutide; shared class safety concerns (gallbladder, rare pancreatitis)[62].
Effects on blood pressure	Semaglutide 2.4 mg was linked to systolic and diastolic blood pressure drops of around 5-7 mmHg and 2-3 mmHg, respectively, in STEP studies[67].	Generally, dose-dependent and quantitatively higher than semaglutide, SURMOUNT-1 demonstrated systolic BP reductions of approximately 6–12 mmHg and diastolic reductions of approximately 3–6 mmHg[62].
Lipid profile improvement	Raises HDL and slightly (~10–20%) lowers triglycerides, LDL-C, and total cholesterol; benefits are correlated with weight loss.	Compared to semaglutide, tirzepatide exhibits bigger increases in HDL and decreases in LDL-C and triglycerides
		(up to −24–28%). SURPASS-2.
Renal outcomes	A 36% decrease in new or worsening nephropathy was shown by SUSTAIN-6, and SELECT also points to worse renal outcomes in obese individuals.	Although no specific renal-outcome trial has yet been finished, post-hoc analysis of SURPASS trials demonstrate notable decreases in albuminuria and a slower fall in eGFR, with effects comparable than GLP-1 RAs.
Real-world effectiveness (RWE)	Several RWE cohorts demonstrate ~8–12% weight loss and ~1.2–1.5% HbA_2c reduction; adherence is lower than RCTs because of coverage and expense[68].	Compared to semaglutide, early real-world datasets show larger decreases in weight (12–20%) and HbA_2c (~2%); adherence patterns seem comparable, although long-term RWE is still evolving.
Cost & market access	Expensive; coverage varies greatly by area. Discontinuation in the real world is frequently associated with affordability[69].	Cost-effectiveness assessments indicate favorable profiles because of increased efficacy; access is improving but remains restricted in many

		countries; prices are frequently comparable or higher depending on the market[68].
Advantages	Proven cardiovascular benefit[65]. Strong HbA_{1c} reduction. Oral formulation available[70]. Extensive clinical evidence basis across diabetes, obesity.	Superior glycemic control. Dual mechanism enhances efficacy[62]. Potential CV benefit.
Limitations	Less glycemic and weight reduction than tirzepatide[29]. Gastrointestinal side effects. Cost/access barriers. Rare but reported risks→ gallbladder disease, pancreatitis, retinopathy complications[71].	Higher rates of GI adverse events at high doses. Limited long-term safety data[29]. No oral formulation.

Future Perspectives: Semaglutide shows strong potential in treating metabolic dysfunction–associated steatohepatitis (MASH/NASH). Phase 3 NEJM trial (2025) confirmed improvement in liver histologic results in patients with moderate-to-severe fibrosis[72]. Earlier Phase 2 trials demonstrated significant NASH resolution, though fibrosis improvement was less consistent[73]. Semaglutide's broader cardiovascular benefit was supported by the SELECT study, which shown that it decreased severe adverse cardiovascular events (MACE) in overweight/obese patients without diabetes. Because of its impacts on weight, insulin resistance, and inflammation, future research is examining its potential in Alzheimer's disease and obesity-driven malignancies[74]. To promote convenience and adherence, better drug delivery methods and advancements in oral formulations are being developed.

Tirzepatide was positioned as a next-generation medication by the SURPASS trials, which showed that it was more benefical than semaglutide at decreasing body weight and HbA1c[75]. Tirzepatide's effect on cardiovascular outcomes is being assessed in the ongoing SURPASS-CVOT trial; new evidence suggests that it is not inferior to dulaglutide and may have additional cardiovascular benefits. There is continuous research on heart failure with preserved ejection fraction (HFpEF) and NASH and the results indicate encouraging reductions in inflammation and liver fat[76]. Oral tirzepatide and fixed-dose combo treatments are potential future advancements that may enhance long-term patient compliance.

CONCLUSION

The utilization of incretin-based therapies for type 2 diabetes has significantly improved when tirzepatide and semaglutide are compared. Both drugs greatly enhance glycaemic management, weight loss, and metabolic health in addition to providing extra heart and kidney protection. Semaglutide is distinct and enhances patient adherence due to its proven safety, cardiovascular benefits, and availability in injectable and oral forms. Tirzepatide is a dual GIP/GLP-1 receptor agonist with good glycemic and weight-loss outcomes. It is a feasible next-generation treatment for people who require stricter care. Both drugs cause gastrointestinal adverse effects, but these are often mild and transient. Long-term trials are still being conducted to examine their benefits in conditions such as obesity, cardiovascular risk reduction, and non-alcoholic steatohepatitis (NASH). In conclusion, semaglutide and tirzepatide both transform the therapy of type 2 diabetes by addressing obesity and hyperglycemia, the two metabolic issues linked to the condition. Their integration into clinical practice should be motivated by patient characteristics, tolerability, accessibility, and comorbidities in order to shift toward a more customized approach to diabetes care.

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List of Abbreviations:

Abbreviations	Full Form
ADA	American Diabetes Association
AKI	Acute Kidney Injury
CVOTs	Cardiovascular Outcome Trials
EASD	European Association for the Study of Diabetes
EMA	European Medicines Agency
GI	Gastrointestinal
GIP	Glucose dependent Insulinotropic Polypeptide
HFpEF	Heart Failure with Preserved Ejection Fraction
MASH	Metabolic Dysfunction-Associated Steatohepatitis
MTC	Medullary Thyroid Carcinoma
NAFLD	Non-Alcoholic Fatty Liver Disease

REFERENCES

1. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. Int J Mol Sci. 2020;21(17):6275.
2. Khanam A, Ahmad S, Husain A. A perspective on the impact of advanced glycation end products in the progression of diabetic nephropathy. *Curr Protein Pept Sci*. 2023;24(1):2-6. doi:10.2174/1389203724666221108120715.
3. Al-Goblan A, Al-Alfi MA, Khan MZ. Mechanism linking diabetes mellitus and obesity. Diabetes Metab Syndr Obes. 2014;7:587-91.
4. Faselis C, Katsimardou A, Imprialos K, Deligkaris P, Kallistratos Dimitriadis K. Microvascular complications of type 2 diabetes mellitus. Curr Vasc Pharmacol.2020;18(2):117-24.
5. Dabelea D, Mayer-Davis EJ, Saydah S, Imperatore G, Linder B, Divers J, et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009: SEARCH for Diabetes in Youth Study. JAMA. 2014;311(17):1778-86.
6. Chen L, Magliano D, Zimmet P. The worldwide epidemiology of type 2 diabetes mellitus: present and future perspectives. Nat Rev Endocrinol. 2012;8:228-36.
7. Levetan C. Oral antidiabetic agents in type 2 diabetes. Curr Med Res Opin. 2007;23(4):945-52.
8. Kumar YG, Kumawat JA, Ashok LD, Pavithra S, Katiyar NS, Punniyakotti S, Thakur A, Sharma D. Formulation and mechanistic evaluation of andrographolide-loaded nano-structured hydrogel for enhanced angiogenic and anti-inflammatory activity in diabetic foot ulcer management. *Int J Drug Deliv Technol*. 2026;16(10 Suppl):819-837. doi:10.25258/ijddt.16.10s.97.
9. Zheng Z, Zong Y, Ma Y, Tian Y, Pang Y, Zhang C, et al. Glucagon-like peptide-1 receptor; mechanisms and advances in therapy. Signal Transduct Target Ther. 2024;9(1):234.
10. H. Sharma, J. Wasim and P. Sharma, "Optimizing Diabetic Retinopathy Detection with Deep Learning and Advanced Image Preprocessing Techniques for High-Accuracy Classification," *2024 1st International Conference on Sustainability and Technological Advancements in Engineering Domain (SUSTAINED)*, Faridabad, India, 2024, pp. 301-307, doi: 10.1109/SUSTAINED63638.2024.11074088.
11. Gieroba B, Kryska A, Sroka-Bartnicka A. Type 2 diabetes mellitus: conventional therapies and future perspectives in innovative treatment. Biochem Biophys Rep. 2025;42:102037.
12. Davies MJ, D'Alessio DA, Fradkin J, Basalely A, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2018: a consensus report by the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2018;41(12):2669-701.
13. Mahapatra MK, Karuppasamy M, Sahoo BM. Semaglutide, a glucagon-like peptide-1 receptor agonist with cardiovascular benefits for management of type 2 diabetes. Rev Endocr Metab Disord. 2022;23(3):521-39.
14. Abiola JO, Oluyemi AA, Idowu OT, Oyinloye OM, Ubah CS, Owolabi OV, et al. Potential role of phytochemicals as glucagon-like peptide 1 receptor (GLP-1R) agonists in the treatment of diabetes mellitus. Pharmaceuticals (Basel). 2024;17:736.
15. Granhall C, Donsmark M, Blicher TM, Søndergaard FL. Oral semaglutide: a novel glucagon-like peptide-1 receptor agonist in type 2 diabetes. Diabetes Ther. 2019;10(1):1-25.
16. Khan AA, Ashfaq S, Pandya S. Semaglutide. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
17. Drucker DJ. Mechanisms of action and therapeutic application of glucagon-like peptide-1. Cell Metab. 2018;27(4):740-56.
18. Yang XD, Yang YY. Clinical pharmacokinetics of semaglutide: a systematic review. Drug Des Devel Ther. 2024;18:2555-70.
19. Gallwitz B, Giorgino F. Clinical perspectives on the use of subcutaneous and oral formulations of semaglutide. Front Endocrinol (Lausanne). 2021;12.
20. Bhandare A, Nannor KM. Bioavailability in drug design and development: a comprehensive review. World J Pharm Res. 2024;13(17):145-8.
21. Aroda VR, Blonde L, Pratley RE. A new era for oral peptides: SNAC and the development of oral semaglutide for the treatment of type 2 diabetes. Rev Endocr Metab Disord. 2022;23(5):979-94.
22. Jensen L, Kupčová V, Arold G, Pettersson J, Hjerpsted JB. Pharmacokinetics and tolerability of semaglutide in people with hepatic impairement. Diabetes Obes Metab. 2018;20(4):998-1105.

23. Papakonstantinou I, Tsioufis K, Katsi V. Spotlight on the mechanism of action of semaglutide. Curr Issues Mol Biol. 2024;46(12):14514-41.
24. Christensen-Petersen I, Leon B, Overgaard S, Bækdal M, Bech Larsen RK, Germeroth J, et al. Absorption, metabolism and excretion of the GLP-1 analogue semaglutide in humans and nonclinical species. Eur J Pharm Sci. 2017;104:31-41.
25. Granhall C, Søndergaard FL, Thomson M, Anderson TW. Pharmacokinetics, safety and tolerability of oral semaglutide in subjects with renal impairment. Clin Pharmacokinet. 2018;57:1571-80.
26. Kommu S, Whitfield P. Semaglutide. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
27. Jude EB, Malecki MT, Gomez Huelgas R, et al. Expert panel guidance and narrative review of treatment simplification of complex insulin regimens to improve outcomes in type 2 diabetes. Diabetes Ther. 2022;13:619-34.
28. Davies MJ, Lingvay I, Rosenstock J, Frias JP, Knop FK, le Roux CW, et al. Semaglutide 2.4 mg once a week in adults with overweight or obesity and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. Lancet. 2021;397(10278):971-84.
29. Frias JP, Lange MA, Aroda VR, Knop FK, Carlsson PO, Leiter LA, et al. Efficacy and safety of once-weekly semaglutide 2.0 mg versus 1.0 mg in patients with type 2 diabetes (SUSTAIN FORTE): a double-blind, randomised, phase 3B trial. Lancet Diabetes Endocrinol. 2021;9(9):563-74.
30. Hansen KBB, Hyldebrandt T, Jensen SL, Lauritsen TV, Bagger P, Thomsen MK, et al. Pharmacokinetics and tolerability of semaglutide in humans: absorption, metabolism, and excretion across species. J Clin Pharmacol. 2017;57(12):1522-31.
31. Davies M, Husain M, Lange MH, Thomsen MK, Aroda VR. Oral semaglutide: a review of the first oral GLP-1 receptor agonist developed for the treatment of type 2 diabetes. Diabetes Obes Metab. 2021;23(5):1182-97.
32. Bækdal TA, Thomsen MH, Kupčová V, et al. Effect of various dosing conditions on the pharmacokinetics of oral semaglutide: a randomised trial in healthy subjects. Diabetes Ther. 2021;12(6):2151-66.
33. Damodaran SP, Thomsen HJ, Bækdal TA, Derving RR, Hjerpsted E, et al. Pharmacokinetics, safety and tolerability of oral semaglutide in subjects with renal impairment. Clin Pharmacokinet. 2018;58(12):1597-607.
34. Pratley RE, Aroda VR, Lingvay I, et al. Semaglutide as a new option for treatment of type 2 diabetes. Lancet Diabetes Endocrinol. 2021;9(11):743-59.
35. Zhang H, Xu Y, Yang Q. Efficacy and safety of semaglutide for type 2 diabetes mellitus: a systematic review and meta-analysis. Front Endocrinol (Lausanne).2021;12:792574.
36. Zinman B, Aroda VR, Buse JB, et al. Efficacy, safety, and tolerability of oral semaglutide added to insulin in type 2 diabetes (PIONEER 8). Diabetes Care.2019;42(12):2262-71.
37. Li A, Su X, Hu S, Wang Y. Efficacy and safety of oral semaglutide in type 2 diabetes mellitus: A systematic review and meta-analysis. Diabetes Res Clin Pract. 2023;198:110605.
38. Rivera FB, Arias-Aguirre E, Aguirre Z, Ybañez MJC, Rubia JMM, Galang DJ, et al. Evaluating the safety profile of semaglutide: an updated meta-analysis. Curr Med Res Opin. 2024;40(9):1495-1514.
39. Smits MM, Van Raalte DH. Safety of semaglutide. Front Endocrinol (Lausanne). 2021;12:645563.
40. Davies MJ, Lingvay I, Aroda VR, Pratley RE, Rosenstock J, Frederich RE, et al. Semaglutide versus comparator in type 2 diabetes. Lancet Diabetes Endocrinol.2017;5(4):275-86.
41. Wilding JPH, Karpe TC, Jensen ST, Knop FK, Lundby-Christensen H, Aroda VR. Once-weekly semaglutide in type 2 diabetes. Diabetes Care. 2019;42(9):1724–32.
42. Bao Y, Fang Y, Wang R, Guo M, Zhang L. Semaglutide in type 2 diabetes. Front Endocrinol (Lausanne). 2021;12:645650.
43. Saunders WH, Aiken CC, McGovern AA, Stamm EB, Jain R. Semaglutide effectiveness in routine care. Diabetes Obes Metab. 2022;24(8):1555-65.
44. Dhirani D, Shahid A, Mumtaz H. A new kind of diabetes medication approved by the FDA: is there hope for obesity? Int J Surg. 2023;109(2):81-2.
45. Chavda VP, Ajabiya J, Teli D, Bojarska J, Apostolopoulos V. Tirzepatide, a new era of dual-targeted treatment for diabetes and obesity: a mini-review. Molecules. 2022;27(13):4315.
46. Liu QK. Mechanisms of action and therapeutic applications of GLP-1 and dual GIP/GLP-1 receptor agonist. Front Endocrinol (Lausanne). 2024;15:

47. Mayendraraj A, Rosenkilde MM, Gasbjerg LS. GLP-1 and GIP receptor signaling in beta cells: a review of receptor interactions and co-stimulation. Peptides. 2022;151:170749.
48. Urva S, Coskun T, Loghin C, Cui X, Roell WC, Alsina-Fernandez J, et al. Clinical pharmacokinetics of the dual GIP and GLP-1 receptor agonist tirzepatide: analyses of data from clinical trials. Clin Pharmacokinet. 2022;61:1315-30.
49. Thomas MK, Urva S, Loghin C, Cui X, Benson C, Haupt A. Pharmacokinetics of tirzepatide, a dual GIP and GLP-1 receptor agonist, in healthy participants and patients with type 2 diabetes mellitus. Clin Pharmacol Drug Dev. 2021;10(7):759-69.
50. Kasra F, Cherian JV. Tirzepatide. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
51. Anderson SL. Tirzepatide for the treatment of adults with type 2 diabetes: an evidence-based review and place in therapy. Diabetes Metab Syndr Obes. 2023;16:3279-91.
52. Infante D. Semaglutide and type 2 diabetes: efficacy, safety, and outcomes. News-Medical. 2024.
53. Sloop KW, Haupt A, Coskun T, et al. Pharmacokinetics, safety, and tolerability of tirzepatide in participants with renal impairment. Clin Pharmacol Drug Dev. 2022;11(5):599-609.
54. Ostołaza LJ, Coskun T, Benson CM, et al. Tirzepatide, a dual GIP and GLP-1 receptor agonist: clinical pharmacology and dosing strategy. Diabetes Obes Metab. 2022;24(7):1243-56.
55. Pfarr A, Gough S, Aroda V, Davies M, et al. Clinical perspectives on tirzepatide: dosing, efficacy, and safety across the SURPASS trials. Diabetes Ther. 2022;13(9):1701-16.
56. Del Prato S, Kahn SE, Pavo I, et al. Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4). Lancet. 2021;398(10313):1811-24.
57. Ludvik B, Giorgino F, Jódar E, et al. Once-weekly tirzepatide versus insulin glargine in type 2 diabetes (SURPASS-5). Lancet Diabetes Endocrinol. 2021;9(7):418-27.
58. Mishra R, Raj R, Elshimy G, Zapata I, Kannan L, Majety P, et al. Adverse events related to tirzepatide. J Endocr Soc. 2023;7(4).
59. Karagiannis T, Avgerinos I, Liakos A, Del Prato S, Matthews DR, Tsapas A, et al. Management of type 2 diabetes with the dual GIP/GLP-1 receptor agonist tirzepatide: a systematic review and meta-analysis. Diabetologia. 2022;65(8):1251-61.
60. Min T, Bain SC, et al. Safety and tolerability of tirzepatide: pooled analysis of the SURPASS clinical program. Diabetes Obes Metab. 2022;24(9):1791-802.
61. Del Prato S, Kahn SE, Pavo I, Weerakkody GJ, Jacob S, Rodríguez A, et al. Tirzepatide versus placebo or semaglutide in patients with type 2 diabetes: pooled analyses of the SURPASS clinical trial program. Diabetes Obes Metab. 2022;24(8):1236-48.
62. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide once weekly for the treatment of obesity in people without diabetes (SURMOUNT-1): a double-blind, randomised, controlled trial. N Engl J Med. 2022;387(3):205-16.
63. Dutta D, Bandyopadhyay D, Ghosh A, Ghosh S. Safety issues with tirzepatide in management of type 2 diabetes and obesity: a narrative review. Diabetes Metab Syndr. 2022;16(10):102656.
64. Heise T, Bain SC, Capehorn M, Nauck MA, Ørsted DD, Lingvay I. Safety and tolerability of tirzepatide in patients with type 2 diabetes: a narrative review. Diabetes Obes Metab. 2022;24(9):1576-90.
65. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al; SUSTAIN-6 Investigators. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2016;375(19):1834-44.
66. Sattar N, McGuire DK, Pavo I, Weerakkody GJ, Nishiyama H, Wiese RJ, et al. Tirzepatide cardiovascular event risk assessment: a pre-specified meta-analysis. Nat Med. 2022;28(3):591-8.
67. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al; STEP 1 Study Group. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 2021;384(11):989-1002.
68. Almandoz JP, Singh S, O'Connor EA, Berkowitz RI, Hoskin MA, Jarolim P, et al. Real-world effectiveness of semaglutide for weight management: a multicenter cohort. Obesity (Silver Spring). 2023;31(5):1128-37.
69. Wadden TA, Tronieri JS, Sugimoto D. Liraglutide and semaglutide: weight-loss agents with cardiometabolic benefits. JAMA. 2023;329(1):70-71.

70. Husain M, Birkenfeld AL, Donsmark M, Dungan K, Eliaschewitz FG, Franco DR, et al; PIONEER 6 Investigators. Oral semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2019;381(9):841-51.
71. Salviato T, Bonetti LR, Mangogna A, Leoncini G, Cadei M, Caprioli F, et al. Microscopic imaging of inflammatory bowel disease and non-IBD colitis on digital slides: the Italian Group-IBD Pathologists experience. Pathol Res Pract. 2020;216(11):153189.
72. Sanyal AJ, Newsome PN, Kliers I, Østergaard LH, Long MT, Kjær MS, et al; ESSENCE Study Group. Phase 3 trial of semaglutide in metabolic dysfunction-associated steatohepatitis. N Engl J Med. 2025;392(21):2089-99.
73. Newsome PN, Buchholtz K, Cusi K, Linder M, Okanoue T, Ratziu V, et al; NN9931-4296 Investigators. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. N Engl J Med. 2021;384(12):1113-24.
74. Lincoff AM, Brown-Frandsen K, Colhoun HM, Deanfield J, Emerson SS, Esbjerg S, et al; SELECT Trial Investigators. Semaglutide and cardiovascular outcomes in obesity without diabetes. N Engl J Med. 2023;389(24):2221-32.
75. Nicholls SJ, Bhatt DL, Buse JB, Del Prato S, Kahn SE, Lincoff AM, et al; SURPASS-CVOT Investigators. Comparison of tirzepatide and dulaglutide on major adverse cardiovascular events in participants with type 2 diabetes and atherosclerotic cardiovascular disease: SURPASS-CVOT design and baseline characteristics. Am Heart J. 2024;267:1-11.
76. Rangnekar SV, Sangwan VK, Jin M, Khalaj M, Szydłowska BM, Dasgupta A, et al. Electroluminescence from megasonically solution-processed MoS2 nanosheet films. ACS Nano 2023:17(17):17516-26.