HANSLIK, Anna, MENDAK, Magdalena, BIAŁEK, Agata, WALCZAK, Agnieszka, HOVAGIMYAN, Adrian, OLSZANECKA, Monika and OLSZANECKI, Tomasz. Tirzepatide - role in obesity, health and physical wellness. Information overview. Quality in Sport. 2025;38:58191. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.38.58191
https://apcz.umk.pl/QS/article/view/58191

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 24.01.2025. Revised: 12.02.2025. Accepted: 13.02.2025 Published: 13.02.2025.

Tirzepatide - role in obesity, health and physical wellness. Information overview

Author's:
Anna Hanslik
ORCID: https://orcid.org/0009-0001-5094-0012
E-mail: ania.han99@gmail.com
University Clinical Hospital in Opole, al. Witosa 26, 45-401 Opole, Poland.

Magdalena Mendak
ORCID: https://orcid.org/0009-0005-7347-1393
E-mail: magda.mendak@gmail.com
University Clinical Hospital in Opole, al. Witosa 26, 45-401 Opole, Poland.

Agata Białek
ORCID: https://orcid.org/0009-0008-3478-4698
E-mail: agataaa.bialek@gmail.com
University Clinical Hospital in Opole, al. Witosa 26, 45-401 Opole, Poland.

Agnieszka Walczak
ORCID: https://orcid.org/0009-0006-5608-1294
E-mail: agnieszka.walczak998@gmail.com
University Clinical Centre in Gdańsk, 80-952 Gdańsk, Poland.

Adrian Hovagimyan
ORCID: https://orcid.org/0009-0007-8091-2817
E-mail: adrianhovagimyan8@gmail.com
University Clinical Hospital in Opole, al. Witosa 26, 45-401 Opole, Poland.

Monika Olszaniecka
ORCID: https://orcid.org/0009-0003-7135-2097
E-mail: olszaneckamonika@gmail.com
Czerniakowski Hospital in Warsaw, Stępińska 19/25, 00-739 Warszawa, Poland.

Tomasz Olszaniecki
ORCID: https://orcid.org/0009-0002-8495-5316
E-mail: tomolszan23@gmail.com
University Clinical Hospital in Opole, al. Witosa 26, 45-401 Opole, Poland.

Abstract

Nowadays there is an increasing number of people with overweight and obesity all around the world. Unhealthy food, sweets and fast foods are available everywhere, that causes self-perpetuating problem. Food restriction is an obvious treatment, but it is difficult to achieve. A certain solution are GLP-1 agonists using to treat type 2 diabetes. Last studies shown that that medicaments may be effective in promoting weight loss. Tirzepatide as a novelty and is a long-acting dual agonist of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. It can be very supportive in the fight against obesity.

Current state of knowledge

High effectiveness of tirzepatide has been observed already in 2021 and has been proven in five phase III clinical trials (SURPASS 1-5). In may 2022 a medicine was approved by the FDA (Food and Drug Administration) and in November 2022 was registered by EMA (European Medicines Agency) for the v of type 2 diabetes. After a lot of reports of successful use for weight loss in patients, doctors began using it off-label to treat obesity.

Scientists created the SURMOUNT development program aims to evaluate the efficacy and safety of tirzepatide as an addition to lifestyle modification (compared with placebo) on chronic weight control in adults with BMI ≥ 27 kg/m2 with accompanying or not type 2 diabetes. Based on the PubMed electronic database, the results will be presented below.

Keywords: tirzepatide, GLP-1, GIP, obesity, type 2 diabetes, SURMOUNT, FDA, EMA

1. Introduction

Obesity is a complex, chronic disease [1], which is an abnormal or excessive accumulation of fat tissue, posing a threat to health. It is a serious condition, which increase the risk of many other diseases such as: coronary heart disease, diabetes, hypertension, stroke, fatty liver disease, obstructive sleep apnea, osteoarthritis and dementia [1]. New study (in 2022) released that more than 1 billion people in the world are living with obesity, which means that one in eight people is obese now [6]:

- 2.5 billion (43%) adults (18 years and older) are overweight - 890 million (16%) of these are living with obesity [6]
- 37 million children under the age of 5 are overweight [6]

- Over 390 million children and adolescents (aged 5–19 years) are overweight - 160 million of these are living with obesity [6]

All over the world, amount of adult obesity has more than doubled since 1990, and has quadrupled among children and adolescents (5 to 19 years of age) [6] [7].

Obesity has achieved epidemic proportions globally. 2.8 million people are dying as a result of being overweight or obese every year [5].

World Obesity Federation published statistics, which depicts that the global level of overweight and obesity will reach $4.32 trillion annually by 2035 if prevention and treatment measures will not be betterment [8]. For this reason, tirzepatide may be a breakthrough in the treatment of this condition and there are high hopes for a new medicament.

2. Diagnosis of obesity

There are various methods that can be used to diagnose obesity. According to the World Health Organization (WHO) the gold standard for diagnosing obesity is the Body Mass Index - BMI. It is calculated as weight in kilograms divided by the height in metres squared. In adults, overweight, or pre-obesity, is defined as a BMI of 25-29.9 kg/m², while a BMI ≥ 30 kg/m² defines obesity and BMI ≥ 40 kg/m² defines severe obesity. [2, 3, 4]

However, this index is very limited (BMI has high specificity 94–96% in men and 98–100% in women but low sensitivity 35–37% in men and 48–50% in women) therefore if the BMI is above the appropriate ethnic guidelines, then there are a number of steps needed to evaluate the importance of that deviation [9].

The first restriction of the BMI is that it does not provide any information how body fat is distributed. Waist circumference is the measure of choice to define central fat distribution and central obesity. Complications, obesity-related health risk and significant increased risk of mortality is depended more on waist circumference (WC), not BMI. This has been confirmed by various researches comparing also other indexes (hip circumference (WHR), weight divided by height (Wt/Height) or WC/height). WC measurement is a cheap and easy method. The cut-off point is various among the countries, in Poland it is ≥ 88cm for woman and ≥ 102 cm for men [10, 11].

A second limitation of the BMI is that it has only a fair correlation with real content of body fat. It is important that measures of fatness should be as close to the actual amount of fat as it is possible. There are many methods. Anthropometric methods are among the oldest. Bioelectric impedance and body density measurements show two-compartment model with fat and non-fat tissue. Dual X-ray absorptiometry (DXA) can measure three sections which including fat, lean, bone and regional location of arms, legs or trunk fat. Ultrasound elastography can outline tissue disease in the liver and kidney [11, 13].

On the other hand there are more precise measurements obtained from magnetic resonance imaging (MRI) and computed tomography (CT) - it provides pictures of body fat [11, 12].

Finally there are genetic, metabolic, physiological or psychological factors involved in the development of obesity. BMI tells us nothing about these aspects, however they are very important and they have a big impact on gain weight [11].

All of these methods improve on the BMI and supply better pictures of fat distribution in the body.

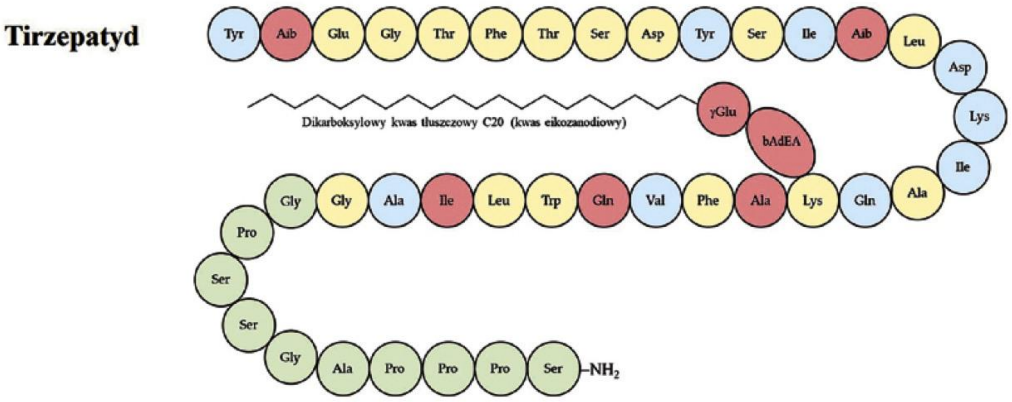
3. Structure of tirzepatide

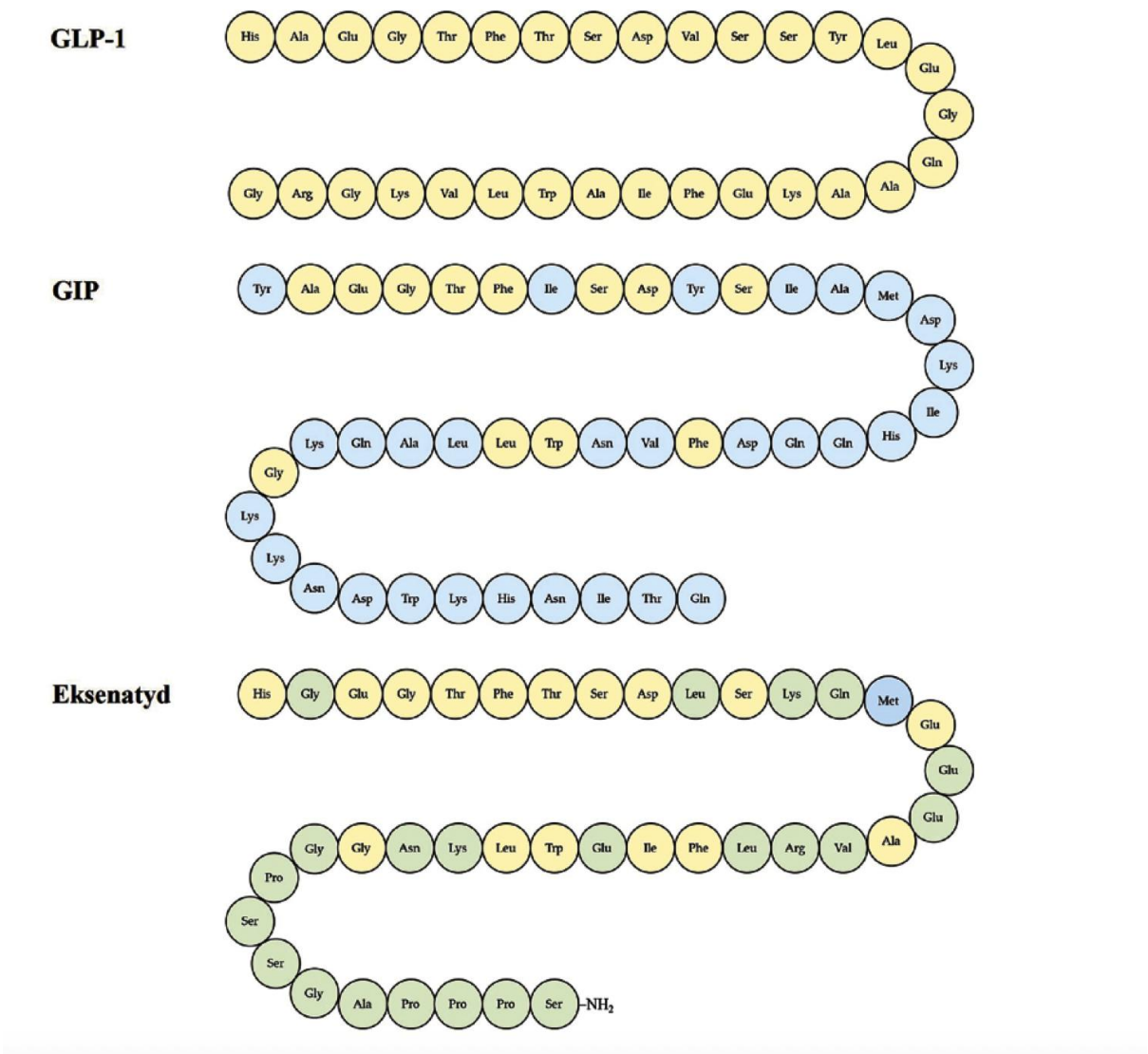
Tirzepatide is a peptide with the formula C225H348N48O68 and a molecular weight of 4813.45 Da. It contains 39 amino-acids in the chain, shows structural similarity to both incretin hormones and activates GLP-1 and GIP receptors simultaneously. The final 10 amino

acids including the amide group at the C-terminus are consistent with the sequence of exenatide [14, 15, 16].

At 2 and 13 position of tirzepatide chain are two non-coding amino-acid residues (α-aminoisobutyric acid; Aib), which are responsible for its resistance to the enzyme dipeptidyl peptidase IV (DPP-4). As a consequence, medicament has a long half-life (6 days) and high affinity for albumin [16, 17, 18].

A C20 dicarboxylic fatty acid residue (eicosanedioic acid) is linked to lysine at position 20 via a hydrophilic linker composed of γ-glutamic acid and bis aminodiethoxyacetyl. This part enhances the binding of the drug to the GLP-1 receptor [16, 18].





Legend:
Ala - Alanine, Arg - Arginine, Asn - Asparagine, Asp - Aspartic Acid, Gln - Glutamine, Gly - Glycine, Glu - Glutamic Acid, His - Histidine, Ile - Isoleucine, Leu - Leucine, Lys - Lysine, Met - Methionine, Phe - Phenylalanine, Pro - Proline, Ser - Serine, Thr - Threonine, Trp - Tryptophan, Tyr - Tyrosine, Val - Valine, Air - α-aminoisobutyric acid, bAdEA - bis- aminodiethoxyacetyl
Color indicates similarity to fragment of another molecule: yellow - GLP-1, blue - GIP, green - exenatide, pink - tirzepatide.
Source: https://stn.ump.edu.pl/prace_naukowe/05_SZ_Tirzepatyd_n.pdf

3.1. Mechanism of action

GIP and GLP-1 are produced in the small intestine cells and secreted in response to ingestion of meals or glucose. GIP and GLP-1 exert theirs effects by binding to specific receptors, the GIP receptor (GIPR) and the GLP-1 receptor (GLP-1R), which belong to the G-protein coupled receptor family. Hormones activate and increase the level of intracellular cyclic adenosine monophosphate (cAMP) in pancreatic β cells, thereby stimulating insulin secretion glucose-dependently (when the glucose concentration exceeds 5 mmol/L). Within the pancreas, GIP and GLP-1 in common promote β-cell proliferation and inhibit apoptosis,

thereby pancreatic β-cell mass is increasing. Moreover GLP-1 suppresses postprandial glucagon secretion significantly and slows down gastric emptying [17, 19, 20].

In addition, GIP and GLP-1 have functions in various biological processes in different tissues. GLP-1 receptors are distributed on α cells of islets and in cell membranes of the brain, blood vessels, heart, lungs, cells of the immune system, intestines, and GIP in tissue fat, heart, pituitary gland, vascular endothelium and adrenal cortex [17, 19, 20].

In adipose tissues, GIP but not GLP-1 facilitates fat deposition. In bone, GIP promotes bone formation while GLP-1 inhibits bone absorption. GIP and GLP-1 are thought to be involved in processes in the brain (memory formation as well as the control of appetite). In addition to these differences, secretion of GIP and GLP-1 and their insulinotropic effects on β-cells have been shown to differ in patients with type 2 diabetes compared to healthy subjects [17, 19, 20].

Common action both incretins enhances the beneficial effect on the treatment of type 2 diabetes and obesity. The action of tirzepatide is based on severe activation of the GLP-1 signaling pathway [21]. It mobilizes insulin secretion dependent on glucose, through the GIP-receptor activity. Due to long half-life, tirzepatide extends the safe blood level of glucose: 71-140 mg/dl [21].

Table 1. Action of incretin hormones

	GLP-1	GIP
	Glucagon-like peptide-1	**Glucose-dependent insulinotropic polypeptide**
Number of acids	39	42
Secretion	L cells of the ileal and colonic mucosa	K cells of the duodenum, jejunal mucosa and proximal ileum
Receptors	Cells of the brain, blood vessels, heart, immune system, intestines, lungs, kidneys, α and β pancreas	Pancreatic β-cells, intestine, adipose tissue, heart, pituitary gland, adrenal cortex, vascular endothelium
Impulse	Carbohydrate-fat meal	—
Insulin secretion (from pancreatic β-cells) effect	Stimulation is glucose dependent	—
Glucagon secretion effect	Decrease	—
Gastric emptying effect	Slow down	Minimal impact

Feeling of satiety effect	Increase	—
Appetite effect	Decrease	—
Postprandial glycemia effect	Decrease	—
Body weight effect	Decrease	—
Pancreatic β-cells effect	Protective effects - cell apoptosis inhibition, proliferation and differentiation stimulation	
Somatostatin secretion (in D-cells of the intestinal mucosa and pancreatic δ-cells) effect	Decrease	

Dose of tirzepatide 15 mg elevates insulin sensitivity in the whole body by 63% and increases pancreatic β cells sensitivity to glucose [21]. The study proved this dependence with participation type 2 diabetes patients by using a hyperglycemic clamp. Compared to the initial state, tirzepatide increased insulin secretion in the first phase by 466%, and in the second by 302% [22].

Tirzepatide reduces appetite and calories intake in a meal. Drug slows down gastric emptying which may retard the rate of glucose absorption after a meal and be beneficial for maintaining proper postprandial glycemia [20, 23].

Treatment with tirzepatide was studied in high-fat diet–fed obese IR mice. The results manifested: body weight reduction, less food intake and plasma leptin devaluation. It also elevated feeling of satiety, cut preference for sweets and a high-fat diet, as well as increased energy expenditure, after the introduction a GIP and GLP-1 agonist [24].

4. Tirzepatide - dosage

The starting dose ought to be 2,5 mg once a week, afterwards dose should be increased after 4 weeks of treatment to 5 mg once a week. If the 5 mg dose is ineffective, it can be increased by another 2,5 mg after another 4 weeks. The maximum dose - 15 mg once a week. There is no specific time of day when the drug should be used [26].

4.1. Tirzepatide - mechanism of action

In pharmacokinetic studies conducted with healthy volunteers, tirzepatide were given in a dose from 0.25 mg to 15 mg. Drug should be injected into the arm, thigh or abdomen

subcutaneously [25, 26]. Average bioavailability is 80% [25, 26]. The time to reach maximum plasma concentration is 8 to 72 hours [25, 26].

The mean steady-state volume of tirzepatide distribution (Vd) is approximately 10.3 L. It is highly bound to plasma albumin (99%) [26].

The average half-life was 5 days, which imply a weekly dosing [25, 26].

Metabolism of tirzepatide: the peptide structure undergoes proteolytic cleavage and the C20 fatty-diacid composition undergoes β-oxidation and amide hydrolysis. Drug is metabolizing into individual amino acids in various tissues (including the liver) and excreted mainly in urine and feces [26, 27].

The pharmacokinetics is not significantly dependent on age, gender, ethnicity, body weight, race, or hepatic or renal impairment [26, 27].

4.2. Tirzepatide - contraidications

Anaphylaxis, angioedema and prior serious hypersensitivity - on the drug or its excipients (sodium chloride, sodium phosphate dibasic heptahydrate) are an absolute contraindications for use [26, 27].

Drug is contraindicated also in patients with Thyroid C-cell tumors. Studies with animal participation demonstrate that tirzepatide caused medullary thyroid carcinoma in rats [27]. However the drug effect in humans is unknown thus patients with a family history of multiple endocrine neoplasia syndrome type-2 (MEN-2) should be careful [26, 27].

GLP-1 receptor agonists are associated with acute pancreatitis. During the tirzepatide clinical trials SURPASS-1 and SURPASS-3 was noticed increase of pancreatic lipase and amylase. And in SURPASS-2 were observed 4 cases of pancreatitis. If pancreatitis is suspected tirzepatide should be immediately discontinue [27].

Acute gallbladder disease is associated with exenatide treatment and it was observed in tirzepatide trial SURPASS-2. Tirzepatide injections may be cause of diabetic retinopathy progression.

These conditions are relative contraindications for tirzepatide therapy (caution is advised) [26, 27].

4.3. Tirzepatide - adverse effects

The primary adverse effects are related to gastrointestinal tract. Decreased appetite is the most common [28].

Nausea, diarrhea, vomiting, acid reflux, dyspepsia, abdominal pain are less frequently [28].

Pancreatitis, cholelithiasis, acute kidney injury, sinus tachycardia are infrequent [28].

Patient using tirzepatide during GLP-1 agents/insulin therapy increase the risk of hypoglycemia [28].

5. Clinical trial results

Tirzepatide has been extensively studied in double-blind, randomised and global controlled phase III clinical trials SURPASS 1-5. These studies proved the long-term efficacy and safety of this treatment in people with type 2 diabetes [29, 30].

Tirzepatide in dose 5 mg, 10 mg, 15 mg was compared with:

- Placebo in monotherapy - SURPASS-1 [30]
- Semaglutide 1 mg (selective GLP-1 RA) (background medication: metformin) - SURPASS-2 [30]

- Insulin degludec (background medication: metformin ± Sodium-glucose Cotransporter-2 [SGLT-2] inhibitor) - SURPASS-3 [30]
- Insulin glargine (background medication: metformin ± SGLT-2 inhibitor or sulfonylurea alone or in combination) - SURPASS-4 [30]
- Placebo (background medication: insulin glargine ± metformin) - SURPASS-5 [30]

Results reveal that the percent of members with tirzepatide achieving an HbA1c > 7,0% with ≥ 5% weight loss (without hypoglycemia) hesitated from 43% to 82% in SURPASS-1-5. Trial with Semaglutide 1 mg (SURPASS-2) achieved 51%, probe with placebo (SURPASS-1/5) reached 4% to 5% and studies with basal insulin (SURPASS-3/4) attained 5% [30, 40].

The scale of participants achieving an HbA1c ≥ 6.5% with ≥ 5% weight loss (without hypoglycaemia) were significantly higher with all tirzepatide doses than with comparators (placebo, Semaglutide and basal insulin) across all five SURPASS trials. Tirzepatide arms ranged from 38% to 78% across trials, the comparator arms achieved 3% for placebo (SURPASS-1/5), 3%-4% for basal insulin (SURPASS-3/4) and 45% for Semaglutide 1 mg (SURPASS-2) [30, 40].

The number of participants attaining an HbA1c ≥ 5,7% with ≥ 5% weight loss (without hypoglycemia) were noticeably superior with all tirzepatide doses. These values ranged from 16% to 51%. Placebo arms were about 1% (SURPASS-1/5), basal insulin arms hesitated between 1-2% (SURPASS-3/4) and Semaglutide 1 mg arms achieved 15% (SURPASS-2) [30, 40].

These endpoints expose the superior efficacy of tirzepatide versus other examined comparators in lowering HbA1c and weight reduction [30, 40].

In conclusion, tirzepatide impact clinically meaningful composite endpoints in therapy type 2 diabetes and in weight loss (without hypoglycemia). These results were consistent across the different populations [30, 40].

6. Clinical trial results continuation

Prevent studies with tirzepatide have shown a strong impact on weight loss. New, targeted trials have been created to investigate safety and direct influence of tirzepatide as an adjunct to lifestyle intervention in adults with BMI ≥ 27 kg/m^2 with or without type 2 diabetes. The SURMOUNT, multicenter, randomized, placebo-controlled, double-blind program, includes four global phase 3 trials. Participants are adults ≥ 18 years old, with a history of ≥ 1 unsuccessful, self-reported dietary effort to lose weight. Excluding factors: type 1 diabetes and adults with a self-reported weight loss > 5 kg 90 days before screening [31].

SURMOUNT-1 (72 weeks duration): evaluation in adults with obesity or overweight. Dosing once a week - 5 mg, 10 mg , 15 mg and placebo (1:1:1:1) [31, 32].

A body-weight reduction in the range ≥ 5% is clinically significant and improves metabolic health. In this trial most of participants (89%-91%) achieved this benchmark receiving 10 mg and 15 mg dose of tirzepatide. Weight reduction of ≥ 10%, ≥ 15%, ≥ 20% was reached by 78%-84%, 67%-71% and 50%-57% participants respectively [31, 32].

For perspective: placebo provided a 3,1% weight reduction, older antiobesity medications approved by the FDA assured approximately 3,0 to 8,6% weight reduction and semaglutide 2,4 mg resulted 12,4% weight reduction [36]. Trial demonstrated additional benefits of using tirzepatide such as: reducing cardiovascular and metabolic risk factors (systolic and diastolic blood pressure, lipid levels), cutting of waist circumstance and transitioning a prediabetes into normoglycemia [31, 32].

SURMOUNT-2 (72 weeks duration): evaluation in adults with obesity and type 2 diabetes. Dosing once a week - 10 mg, 15 mg and placebo (1:1:1) [31, 34].

Both tirzepatide doses achieved all endpoints throughout the whole trial [35].
Mean body weight reductions achieved 12,8% participants (10 mg dose), 14,7% (15 mg dose), compared to placebo 3,2% [35].
Amount of participants who have reached at least ≥ 15% body weight reduction: 40% (10 mg) and 48% (15 mg), compared to placebo - 3% [35].
HbA1c level < 5,7% was achieved by a 46% participants (10 mg dose) nad 49% members (15 mg dose), compared to placebo - 4% [35].
Moreover, this trial demonstrated significantly reduction in systolic blood pressure, fasting triglycerides and non-HDL-cholesterol [35].

SURMOUNT-3 (72 weeks duration): evaluation in adults with obesity or overweight and comorbidity after lifestyle modification. Maximum tolerated dose once a week - 10 mg or 15 mg and placebo (1:1) [31, 36].
During the 12-week intensive lifestyle modification qualified participants lost 6,9% of body weight. Members, who maintained 80% of their weight loss during the lifestyle intervention reached 94% in the tirzepatide team, compared to 43,8% in the placebo group [37].
Total weight reduction, during the whole study, ranged 24,3% with tirzepatide and 4,5% with placebo [37].
After 72-weeks of treatment, mean weight reduction was 18,4% in the tirzepatide group, compared to 2,5% with placebo. Endpoint of 5% body weight reduction achieved 87,5% participants in tirzepatide team, compared to 16,5% with placebo [37].
Trial demonstrated accompanying waist circumference decreasing, blood pressure improving, fasting lipid levels and reducing HbA1c [37].

SURMOUNT-4 (88 weeks duration): evaluation in adults with obesity or overweight and comorbidity treating for a 36 weeks lead-in period with tirzepatide followed by a 52-week double-blind placebo period. Maximum tolerated dose once a week - 10 mg or 15 mg and placebo (1:1) [31, 38].
After the 36-week lead-in period treatment participants achieved a mean 20,9% weight reduction. Subsequently, between 36 and 88-week of trial, weight decreased by another -5,5% with tirzepatide, and increased 14% with placebo [39].
Overall, 89,5% of participants (after the 88-week treatment with tirzepatide) maintained at least 80% of the weight loss obtained during the lead-in period and only 16,6% members maintained that weight loss with placebo [39].
Summing up, a mean weight reduction throughout whole study was 25,3% for tirzepatide and 9,9% for placebo [39].

7. Summary

Nowadays, obesity is a serious, dangerous and still growing problem. Current medications and attempt of insertion a diet and exercises are insufficient. New therapies and medicaments are still developing.

A certain breakthrough is a tirzepatide - subcutaneously medication, administered once a week.

Several years of trials have proven invaluable assistance of tirzepatide in type 2 diabetes treatment and complications (SURPASS trials), as well as decreasing level of obesity over the world (SURMOUNT trials). Trials SURMOUNT-1 and -2 reveal that this drug seems to be a promising therapeutic option, providing effective glycemic control, weight loss and improvement of cardiometabolic parameters, making it a valuable tool in the treatment of type 2 diabetes and obesity. It is also much more effective than the older GLP-1 analogues and leads to greater weight loss.

Some experts believe that drugs for obesity should be used chronically, similarly to diabetes or hypertension. This thesis is also supported by observations from the previously mentioned SURMOUNT-4 study. Patients of tirzepatide group achieved a spectacular weight loss at the end of the study, relative to the second group received placebo (where noticed increase in body weight). Observations say that patients with diagnosed obesity, starting the drug for several months is pointless and does not bring lasting effects. For the time being, tirzepatide is a future in the daily treatment of bariatric patients but SURMOUNT-3 trial proved that it has to be connected with lifestyle change, a low-calorie diet and increased physical activity (together is the most effective).

However, elimination obesity over the world will solve many health problems and it will be a great opportunity to improve a patient's healthy life years, quality-adjusted life years and health-related quality of life so let's use this valuable tool - breakthrough drug tirzepatide in treatment and fight with obesity epidemic.

Disclosures

Author's contribution

Conceptualization - Anna Hanslik;
Methodology - Magdalena Mendak;
Software - Agnieszka Walczak;
Analysis - Agata Białek;
Investigation - Adrian Hovagimyan;
Resources - Monika Olszaniecka;
Data curation - Tomasz Olszaniecki, Adrian Hovagimyan;
Writing - Anna Hanslik;
Preparation - Anna Hanslik;
Visualization - Magdalena Mendak, Monika Olszaniecka;
Supervision - Agnieszka Walczak;
Project administration - Anna Hanslik, Agata Białek; receiving funding not applicable.
All authors have read and agreed with the published version of the manuscript.

Funding Statement:
This Research received no external funding.

Institutional Review Board Statement:
Not applicable

Informed Consent Statement:
Not applicable.

Data Availability Statement:
The authors confirm that the data supporting the findings of this study are available within the article's bibliography

Conflicts of Interests:
Authors declare no conflict of interests.

References

1. Mahmood Safaei, Elankovan, Sundararajan, Maha Driss, Wadii Boulila, Azrulhizam Shapi'i, 2021, A systematic literature review on obesity: Understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity DOI: 10.1016/j.compbiomed.2021.104754
2. Connor B. Weir, Arif Jan., 2023, BMI Classification Percentile And Cut Off Points Bookshelf ID: NBK541070
3. Marie-Eve Piché, André Tchernof, Jean-Pierre Després, 2020, Obesity Phenotypes, Diabetes, and Cardiovascular Diseases DOI: 10.1161/CIRCRESAHA.120.316101
4. B. Conway, A. Rene, 2004, Obesity as a disease: no lightweight matter DOI: 10.1111/j.1467-789X.2004.00144.x
5. THE GLOBAL HEALTH OBSERVATORY; Obesity https://www.who.int/data/gho/indicator-metadata-registry/imr-details/3420
6. 2024, World Health Organization; Obesity and overweight https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
7. 2024, World Health Organization; One in eight people are now living with obesity https://www.who.int/news/item/01-03-2024-one-in-eight-people-are-now-living-with-obesity
8. World Obesity; Economic impact of overweight and obesity to surpass $4 trillion by 2035 https://www.worldobesity.org/news/economic-impact-of-overweight-and-obesity-to-surpass-4-trillion-by-2035
9. A Romero-Corral, V K Somers, J Sierra-Johnson, R J Thomas, M L Collazo-Clavell, J Korinek, T G Allison, J A Batsis, F H Sert-Kuniyoshi, 2008, F Lopez-Jimenez Accuracy of Body Mass Index to Diagnose Obesity In the US Adult Population DOI: 10.1038/ijo.2008.11
10. Piotr Jankowski, Paweł Kozieł, Andrzej Pająk, 2023 ,Body mass index and waist circumference in patients with established coronary artery disease over a 20-year period DOI: 10.5603/CJ.a2023.0001
11. George A. Bray, 2023, Beyond BMI DOI: 10.3390/nu15102254
12. Daniela Franz, Jan Syväri, Dominik Weidlich, Thomas Baum, Ernst J Rummeny, Dimitrios C Karampinos, 2018, Magnetic Resonance Imaging of Adipose Tissue in Metabolic Dysfunction DOI: 10.1055/a-0612-8006
13. Hongbo Dong, Hong Cheng, Jingfan Xiong, Li Liu, Yiwen Huang, Xinying Shan, Hongmin Fan, Xi Wang, Xia Wang, Pei Xiao, Fangfang Chen, Jie Mi, 2024, Body fat variation and redistribution across different stages of life measured by dual-energy x-ray absorptiometry DOI: 10.7189/jogh.14.04247
14. 2022, PubChem CID 163285897 https://pubchem.ncbi.nlm.nih.gov/compound/163285897
15. 2022, Tirzepatide https://www.guidetopharmacology.org/GRAC/LigandDisplayForward?tab=structure&ligandId=11429
16. Gabriela Anglart1, Laura Janik1, Katarzyna Dettlaff, 2023, Tirzepatyd – nowy analog hormonów inkretynowych https://stn.ump.edu.pl/prace_naukowe/05_SZ_Tirzepatyd_n.pdf
17. Thinzar Min, Stephen C. Bain, 2020, The Role of Tirzepatide, Dual GIP and GLP-1 Receptor Agonist, in the Management of Type 2 Diabetes: The SURPASS Clinical Trials DOI: 10.1007/s13300-020-00981-0
18. Yutaka Seino, Mitsuo Fukushima, Daisuke Yabe, 2010, GIP and GLP-1, the two incretin hormones: Similarities and differences DOI: 10.1111/j.2040-1124.2010.00022.x

19. Qiyuan Keith Liu, 2024, Mechanisms of action and therapeutic applications of GLP-1 and dual GIP/GLP-1 receptor agonists DOI: 10.3389/fendo.2024.1431292
20. Christophe De Block MD, Clifford Bailey PhD, Carol Wysham MD, Andrea Hemmingway PhD, Sheryl Elaine Allen MD, Jennifer Peleshok PhD, 2022, Tirzepatide for the treatment of adults with type 2 diabetes: An endocrine perspective DOI: 10.1111/dom.14831
21. Michael A. Nauck & David A. D'Alessio , 2022, Tirzepatide, a dual GIP/GLP-1 receptor co-agonist for the treatment of type 2 diabetes with unmatched effectiveness regrading glycaemic control and body weight reduction DOI: 10.1186/s12933-022-01604-7
22. SUMMARY OF PRODUCT CHARACTERISTICS https://www.ema.europa.eu/en/documents/product-information/mounjaro-epar-product-information_en.pdf
23. Tim Heise, J. Hans DeVries, Shweta Urva, Jing Li, Edward J. Pratt, Melissa K. Thomas, Kieren J. Mather, Chrisanthi A. Karanikas, Julia Dunn, Axel Haupt, Zvonko Milicevic, Tamer Coskun, 2023, Tirzepatide Reduces Appetite, Energy Intake, and Fat Mass in People With Type 2 Diabetes DOI: 10.2337/dc22-1710
24. Ricardo J. Samms, Michael E. Christe, Kyla A.L. Collins, Valentina Pirro, Brian A. Droz, Adrienne K. Holland, Jessica L. Friedrich, Samantha Wojnicki, Debra L. Konkol, Richard Cosgrove, Ellen P.S. Conceição Furber, Xiaoping Ruan, Libbey S. O'Farrell, Annie M. Long, Mridula Dogra, Jill A. Willency, Yanzhu Lin, Liyun Ding, Christine C. Cheng, Over Cabrera, Daniel A. Briere, Jorge Alsina-Fernandez, Ruth E. Gimeno, Julie S. Moyers, Tamer Coskun, Matthew P. Coghlan, Kyle W. Sloop, and William C. Roell, 2021, GIPR agonism mediates weight-independent insulin sensitization by tirzepatide in obese mice DOI: 10.1172/JCI146353
25. Karen Schneck, Shweta Urva, 2024, Population pharmacokinetics of the GIP/GLP receptor agonist tirzepatide https://doi.org/10.1002/psp4.13099
26. Khashayar Farzam, Preeti Patel., 2024, Tirzepatide https://www.ncbi.nlm.nih.gov/books/NBK585056/
27. Baptist Gallwitz, 2022, Clinical perspectives on the use of the GIP/GLP-1 receptor agonist tirzepatide for the treatment of type-2 diabetes and obesity DOI: 10.3389/fendo.2022.1004044
28. Rahul Mishra, Rishi Raj, Ghada Elshimy, Isain Zapata, Lakshmi Kannan, Priyanka Majety, Dinesh Edem, Ricardo Correa, 2023, Adverse Events Related to Tirzepatide DOI: 10.1210/jendso/bvad016
29. Michael A. Nauck & David A. D'Alessio, 2022, Tirzepatide, a dual GIP/GLP-1 receptor co-agonist for the treatment of type 2 diabetes with unmatched effectiveness regrading glycaemic control and body weight reduction DOI: 10.1186/s12933-022-01604-7
30. Ildiko Lingvay MD, Alice YY. Cheng MD, Joshua A. Levine MD, Elisa Gomez-Valderas MSc, Sheryl E. Allen MD, Kari Ranta MD, Amelia Torcello-Gómez PhD, Vivian T. Thieu PhD, 2022, Achievement of glycaemic targets with weight loss and without hypoglycaemia in type 2 diabetes with the once-weekly glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist tirzepatide: A post hoc analysis of the SURPASS-1 to -5 studies DOI: 10.1111/dom.14943
31. Carel W. le Roux, Shuyu Zhang, Louis J. Aronne, Robert F. Kushner, Ariana M. Chao, Sriram Machineni, Julia Dunn, Farai B. Chigutsa, Nadia N. Ahmad, Mathijs C. Bunck, 2022, Tirzepatide for the treatment of obesity: Rationale and design of the SURMOUNT clinical development program DOI: 10.1002/oby.23612

32. Ania M. Jastreboff, M.D., Ph.D., Louis J. Aronne, M.D., Nadia N. Ahmad, M.D., M.P.H., Sean Wharton, M.D., Pharm.D., Lisa Connery, M.D., Breno Alves, M.D., Arihiro Kiyosue, M.D., Ph.D., Shuyu Zhang, M.S., Bing Liu, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Adam Stefanski, M.D., 2022, Tirzepatide Once Weekly for the Treatment of Obesity https://www.nejm.org/doi/10.1056/NEJMoa2206038
33. A Study of Tirzepatide (LY3298176) in Participants With Obesity or Overweight (SURMOUNT-1) https://clinicaltrials.gov/study/NCT04184622
34. Prof W Timothy Garvey MD, Juan P Frias, MD, Ania M Jastreboff, MD, Prof Carel W le Roux, MD, Prof Naveed Sattar, MD, Diego Aizenberg, MD, 2023, Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial DOI: 10.1016/S0140-6736(23)01200-X
35. A Study of Tirzepatide (LY3298176) in Participants With Type 2 Diabetes Who Have Obesity or Are Overweight (SURMOUNT-2) https://clinicaltrials.gov/study/NCT04657003
36. A Study of Tirzepatide (LY3298176) In Participants After A Lifestyle Weight Loss Program (SURMOUNT-3) https://clinicaltrials.gov/study/NCT04657016
37. Thomas A. Wadden, Ariana M. Chao, Sriram Machineni, Robert Kushner, Jamy Ard, Gitanjali Srivastava, Bruno Halpern, Shuyu Zhang, Jiaxun Chen, Mathijs C. Bunck, Nadia N. Ahmad & Tammy Forrester, 2023, Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial DOI: 10.1038/s41591-023-02597-w
38. A Study of Tirzepatide (LY3298176) in Participants With Obesity or Overweight for the Maintenance of Weight Loss (SURMOUNT-4) https://clinicaltrials.gov/study/NCT04660643
39. Louis J. Aronne, MD, Naveed Sattar, MD, Deborah B. Horn, DO, MPH, Harold E. Bays, MD, Sean Wharton, MD, Wen-Yuan Lin, MD, PhD, Nadia N. Ahmad, MD, MPH, Shuyu Zhang, MSc, Ran Liao, PhD, Mathijs C. Bunck, MD, PhD, Irina Jouravskaya, MD, PhD, Madhumita A. Murphy, MD, 2023, Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial DOI: 10.1001/jama.2023.24945
40. Julio Rosenstock, Luis Vázquez, Stefano Del Prato, Denise Reis Franco; Govinda Weerakkody, Biyue Dai, Laura Fernández Landó, Brandon K. Bergman, Angel Rodríguez, 2023, Achieving Normoglycemia With Tirzepatide: Analysis of SURPASS 1–4 Trials DOI: 10.2337/dc23-0872