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Review Article

Glucagon-Like Peptide-1–Based Agonists as Novel Targets In Obesity Management: Mechanistic Pathways and Adverse Effects

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Summary

Obesity is a persistent, recurring condition resulting from dysregulated gut-brain-adipose signaling and disrupted energy balance. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have proven to be highly effective pharmacotherapies, facilitating an average weight reduction of 10–25% in individuals with obesity through coordinated effects on hypothalamic appetite pathways, mesolimbic reward systems, gastrointestinal motility, pancreatic islet activity, and hepatic–adipose metabolism. They may lower the risk of serious cardiovascular events and protect the kidneys in people at high risk, which supports GLP-1-based therapy as a key part of lowering the risk of cardiometabolic disease. However, GLP-1/GIP agonism is also linked to a specific set of negative side effects, such as nausea, vomiting, diarrhea, and constipation that get worse with higher doses, as well as a higher risk of gallbladder disease, pancreatitis, and gastrointestinal problems. This mini-review emphasize on the mechanistic pathways linking GLP-1/GIP agonism to weight loss and cardiometabolic benefits and examines the pathophysiologic basis of key adverse effects to guide individualized use of semaglutide and tirzepatide in endocrinology and obesity practice.

Keywords: Glucagon-like peptide-1 receptor agonists, Obesity, Semaglutide, Tirzepatide

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Introduction

GLP-1 biology and dysregulation in obesity

Endogenous GLP-1 is secreted from enteroendocrine L-cells in the distal small intestine and colon in response to nutrient ingestion, then acts as an incretin hormone to enhance glucose-dependent insulin secretion, suppress glucagon and slow gastric emptying, while also activating vagal afferents and central pathways mediating satiety.[1-3] In obesity and insulin-resistant states, impaired post-prandial GLP-1 secretion and alterations in GLP-1 receptor signaling at the level of the hypothalamus and vagus contribute to blunted satiety and maintenance of positive energy balance, providing a strong rationale for pharmacologic GLP-1R activation as a disease-modifying strategy.[4]

Native GLP-1 is rapidly degraded by dipeptidyl peptidase-4 (DPP-4), yielding a plasma half-life of only a few minutes, whereas therapeutic agonists such as semaglutide incorporate amino-acid substitutions and albumin-binding side chains to resist DPP-4 and neutral endopeptidase degradation, allowing once-weekly administration with sustained receptor engagement. Tirzepatide is engineered as a single peptide with agonist activity at both GIP and GLP-1 receptors, thereby engaging complementary incretin pathways that together amplify insulin secretion and weight loss beyond that achievable by selective GLP-1R agonism alone.[5,6]

Tirzepatide's dual agonism at GIP and GLP-1 receptors results in superior average weight loss compared to semaglutide at doses sanctioned for type 2 diabetes and obesity, with mean reductions nearing or surpassing 20% of baseline body weight in dedicated obesity trials. Preclinical models suggest that GIP receptor activation in adipocytes improves lipid metabolism and may facilitate browning and thermogenesis in specific depots, thereby enhancing GLP-1-mediated reductions in energy intake.[7-9]

Clinical data comparing tirzepatide and semaglutide show that tirzepatide leads to bigger drops in body weight, glycated hemoglobin, and some lipid parameters in people with type 2 diabetes. This is in line with a synergistic incretin effect.[9,10] Nonetheless, the exact relative impact of GIP compared to GLP-1 agonism on human weight reduction continues to be a subject of ongoing research and will guide the creation of next-generation multi-agonists that integrate GLP-1 withGIP, glucagon, amylin, or other gastrointestinal hormones.

Regulation of body weight and central appetite circuits

GLP-1 receptors are abundantly present in hypothalamic nuclei, such as the arcuate nucleus, paraventricular nucleus, and ventromedial hypothalamus, where agonist binding increases the activity of anorexigenic POMC/CART neurons and decreases the activity of orexigenic NPY/AgRP neurons.[4] Chronic GLP-1R activation not

only diminishes acute hunger by shifting the balance of melanocortin signaling toward satiety, but it also seems to lower the defended body-weight set point, facilitating sustained weight loss rather than temporary reductions.[11,12]

In addition to homeostatic feeding circuits, GLP-1RAs target mesolimbic reward pathways, including the ventral tegmental area and nucleus accumbens, diminishing dopamine release and reward valuation in response to food stimuli. Human studies utilizing semaglutide reveal diminished activation of reward regions and heightened engagement of cognitive control networks on functional MRI. This is accompanied by a reduction in energy intake and a preference shift towards less energy-dense food options, highlighting the dual homeostatic and hedonic mechanisms of weight reduction.[2,13]

Peripheral mechanisms Emptying the stomach and moving the gut

When GLP-1 receptors are activated in the gastrointestinal tract, they slow down gastric emptying by raising pyloric tone and lowering antral and duodenal motility. This creates a "ileal brake" that keeps nutrients in the distal small intestine longer and boosts signals of fullness. This effect reduces post-prandial glucose fluctuations and immediate caloric intake; however, partial tachyphylaxis to the gastric-emptying aspect occurs over weeks, with central appetite modulation remaining the primary factor for long-term weight loss.[14,15]

Effects on pancreatic islets, liver, and fat tissue

At the pancreatic islet, GLP-1R activation enhances glucose-dependent insulin secretion, suppresses glucagon release during hyperglycemia and euglycemia, and may facilitate beta-cell survival and function, thereby improving glycemic control with a minimal inherent risk of hypoglycemia.[16,17] In tirzepatide, simultaneous GIP receptor agonism further amplifies insulinotropic effects, especially at elevated glucose concentrations, and may enhance post-prandial beta-cell responsiveness relative to GLP-1-selective agonists.GLP-1–based agonists enhance hepatic insulin sensitivity, diminish de novo lipogenesis, and selectively reduce visceral and ectopic fat depots.[18] This is linked to decreased inflammatory signaling and the improvement of metabolic-associated steatohepatitis.[19,20] These alterations in adipose distribution and hepatic lipid content significantly influence the observed enhancements in blood pressure, lipid profiles, and overall cardiometabolic risk in obesity trials involving semaglutide and tirzepatide.

Cardiometabolic and cardiovascular outcomes

GLP-1RAs, such as semaglutide, liraglutide, and dulaglutide, have consistently shown to lower the risk of major adverse cardiovascular events (MACE) in people with type 2 diabetes and a high risk of heart disease.[6,21,22] This is likely because they have effects on weight, blood pressure, atherogenic lipids, inflammation, and direct vascular actions.[23] Recent data also show that semaglutide can lower the risk of heart disease in people who are overweight or obese and already have heart disease, even if they don't have diabetes.[8,21,24] This expands the cardioprotective paradigm to primary obesity care. Renal advantages of GLP-1 receptor agonists encompass the mitigation of albuminuria progression and a decelerated reduction in estimated glomerular filtration rate, potentially indicative of hemodynamic, metabolic, and anti-inflammatory influences within the kidney.[25-27] These cardiorenal benefits bolster the case for GLP-1-based agonists as essential components in the treatment of obesity complicated by cardiometabolic disorders.

Clinical effectiveness in obesity

In randomized phase III obesity trials, individuals with overweight or obesity receiving once-weekly semaglutide 2.4 mg experience a mean weight loss of approximately 10–15%, with a significant proportion achieving reductions of ≥5% and ≥10% in body weight compared to lifestyle modification alone.[8,23] These weight changes are associated with clinically significant improvements in blood pressure, triglycerides, glycemic control, indicators of fatty liver disease, and health-related quality of life.[4]

When given at doses aimed at obesity, tirzepatide causes even bigger weight losses, with average losses of about 15–20% or more and a large number of patients losing 20% or more of their weight when treatment continues.[10] Stopping either semaglutide or tirzepatide causes most patients to gain some of the weight they lost back. This is because the neuroendocrine and behavioral factors that cause obesity come back. This shows that drug treatment for obesity, like drug treatment for high blood pressure or high cholesterol, usually needs to be long-term.

Adverse effects

Gastrointestinal effects

The most frequent adverse effects of semaglutide and tirzepatide are gastrointestinal—nausea, vomiting, diarrhea and constipation—which arise from exaggerated physiological actions of GLP-1 on gut motility and central emetic centers. Slowed gastric emptying increases gastric distension and activation of vagal afferents projecting to the area postrema and nucleus tractus solitarius, producing nausea and, at higher receptor occupancy, emesis.[28-31]

Diarrhea and, conversely, constipation reflect altered small-intestinal transit, changes in intestinal fluid secretion and modulation of enteric neural circuits under sustained incretin stimulation. These adverse effects are typically dose-dependent and most prominent during dose escalation, so gradual titration, smaller meals, avoidance of high-fat foods and mindful hydration are key mechanistic strategies to improve tolerability while

maintaining therapeutic efficacy.[32]

Bile and gallbladder disease

GLP-1RA therapy is associated with an increased incidence of gallbladder-related events, including cholelithiasis and cholecystitis, particularly at higher doses used for obesity and in the setting of rapid weight loss. Rapid fat loss promotes cholesterol supersaturation of bile and sludge formation, while GLP-1–mediated reductions in cholecystokinin-driven gallbladder contraction lead to biliary stasis, together creating a lithogenic environment.[33-35]

Pancreatitis and pancreatic safety

Elevations in amylase and lipase are relatively common but usually asymptomatic during GLP-1RA therapy; however, rare cases of acute pancreatitis have been reported, raising concerns about direct pancreatic effects.[36,37] Proposed mechanisms include incretin-mediated alterations in ductal secretion, low-grade acinar cell stress and inflammatory responses in predisposed individuals, particularly those with gallstones, severe hypertriglyceridemia or prior pancreatitis.[34]

Large randomized trials and meta-analyses generally show low absolute rates of pancreatitis and no major class-wide signal of marked risk increase, but cautious avoidance or close monitoring is advised in patients with a history of pancreatitis.[38] When clinically suspected, GLP-1RA therapy should be discontinued and alternative weight-management strategies considered.

Gastroparesis, bowel obstruction and motility disorders

Because GLP-1RAs slow gastric emptying and modify small-bowel motility, rare but clinically important cases of symptomatic gastroparesis and intestinal obstruction have been described, especially with high-dose, long-acting formulations. Mechanistically, excessive suppression of vagal efferent activity and inhibition of antral and duodenal contractility can produce functional obstruction-like physiology in individuals with underlying motility disorders or altered surgical anatomy.[39]

Patients who develop persistent vomiting, severe bloating, or early satiety with significant nutritional compromise should be evaluated for gastroparesis or partial obstruction, and withdrawal of the GLP-1RA often leads to partial or complete resolution of symptoms. Pre-existing gastroparesis, connective-tissue disease or major upper-GI surgery warrants cautious use or selection of alternative obesity therapies.[40,41]

Thyroid, kidney and long-term safety considerations

Rodent studies show C-cell hyperplasia and medullary thyroid carcinoma with some GLP-1RAs, but human epidemiologic data have not demonstrated a clear increase in medullary thyroid carcinoma, although long-term surveillance continues.[42,43] Because of this theoretical risk and species differences in C-cell biology, GLP-1RAs are contraindicated in patients with personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2.[44]

GLP-1RAs can cause modest increases in heart rate and, in the context of severe vomiting or diarrhea, contribute to volume depletion and acute kidney injury, underscoring the need for hydration counselling and temporary drug interruption during acute illness.[24,27] Overall, the balance of evidence favors a net renal and cardiovascular benefit when these agents are used with appropriate patient selection and monitoring.[21,22,26]

Conclusion

From an endocrine and obesity-medicine perspective, semaglutide and tirzepatide represent mechanistically rational therapies that target both homeostatic and hedonic components of obesity, yielding weight loss magnitudes historically seen only with bariatric surgery in some patients. Their use should be embedded in a chronic disease model, with careful patient selection, slow dose escalation, proactive management of gastrointestinal and biliary risks and shared decision-making about long-term therapy.

Future research priorities include identifying biomarkers of response and intolerance, delineating the relative contributions of GLP-1 versus GIP pathways, optimizing combination strategies with lifestyle, bariatric surgery and other pharmacotherapies, and developing multi-agonists that further exploit gut–brain–adipose biology with improved tolerability. Such advances are likely to consolidate incretin-based therapies as a central pillar of obesity and cardiometabolic disease management in the coming decade.

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Competing Interests

The authors declare no conflict of interest.

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References

1. Ajabnoor GMA, Hashim KT, Alzahrani MM, Alsuheili AZ, Alharbi AF, Alhozali AM, et al. The possible effect of the long-term use of glucagon-like peptide-1 receptor agonists (GLP-1RA) on Hba1c and lipid profile in type 2 diabetes mellitus: a

retrospective study in KAUH, Jeddah, Saudi Arabia. Diseases. 2023;11(1):50. doi: 10.3390/diseases11010050
2. Kurkin D, Bakulin D, Morkovin E, Petrov V, Strygin A, Koryanova K, et al. Physiology and pharmacology of glucagon-like peptide-1 receptor. Pharmacy & Pharmacology. 2024;11(4): 347-80. doi:10.19163/2307-9266-2023-11-4-347-380
3. Müller TD, Finan B, Bloom SR, D'Alessio D, Drucker DJ, Flatt PR, et al. Glucagon-like peptide 1 (GLP-1). Mol Metab. 2019;30:72-130. doi: 10.1016/j.molmet.2019.09.010
4. Park J-y, Kim H-L, Kwon S-H, Lee E-K. Efficacy and safety of GLP-1 receptor agonist for adults with overweight and obesity: a systematic review and bayesian network meta-analysis of randomized controlled trials. Yakhak Hoeji. 2025;69(3):240-55. doi: 10.17480/psk.2025.69.3.240
5. Antza C, Nirantharakumar K, Doundoulakis I, Tahrani AA, Toulis KA. The development of an oral GLP-1 receptor agonist for the management of type 2 diabetes: evidence to date. Drug Des Devel Ther. 2019;13:2985-96. doi: 10.2147/dddt.S166765
6. Bertoccini L, Baroni MG. GLP-1 Receptor Agonists and SGLT2 Inhibitors for the Treatment of Type 2 Diabetes: New Insights and Opportunities for Cardiovascular Protection. Adv Exp Med Biol. 2021;1307:193-212. doi: 10.1007/5584_2020_494
7. Wadden TA, Bailey TS, Billings LK, Davies M, Frias JP, Koroleva A, et al. Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial. Jama. 2021;325(14):1403-13. doi: 10.1001/jama.2021.1831
8. Rubino D, Abrahamsson N, Davies M, Hesse D, Greenway FL, Jensen C, et al. Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity: The STEP 4 Randomized Clinical Trial. Jama. 2021;325(14):1414-25. doi: 10.1001/jama.2021.3224
9. Rosenstock J, Wysham C, Frías JP, Kaneko S, Lee CJ, Fernández Landó L, et al. Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial. Lancet. 2021;398(10295):143-55. doi: 10.1016/s0140-6736(21)01324-6
10. Frías JP, Davies MJ, Rosenstock J, Pérez Manghi FC, Fernández Landó L, Bergman BK, et al. Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes. N Engl J Med. 2021;385(6):503-15. doi: 10.1056/NEJMoa2107519
11. Drucker DJ. Mechanisms of Action and Therapeutic Application of Glucagon-like Peptide-1. Cell Metab. 2018;27(4):740-56. doi: 10.1016/j.cmet.2018.03.001
12. Bliss ES, Whiteside E. The Gut-Brain Axis, the Human Gut Microbiota and Their Integration in the Development of Obesity. Front Physiol. 2018;9:900. doi: 10.3389/fphys.2018.00900
13. Hayes MR, Schmidt HD. GLP-1 influences food and drug reward. Curr Opin Behav Sci. 2016;9:66-70. doi: 10.1016/j.cobeha.2016.02.005
14. Marathe CS, Rayner CK, Jones KL, Horowitz M. Effects of GLP-1 and incretin-based therapies on gastrointestinal motor function. Exp Diabetes Res. 2011;2011:279530. doi: 10.1155/2011/279530
15. Arunachala Murthy T, Chapman M, Jones KL, Horowitz M, Marathe CS. Inter-relationships between gastric emptying and glycaemia: Implications for clinical practice. World J Diabetes. 2023;14(5):447-59. doi: 10.4239/wjd.v14.i5.447
16. Zhang Y, Parajuli KR, Fava GE, Gupta R, Xu W, Nguyen LU, et al. GLP-1 Receptor in Pancreatic α-Cells Regulates Glucagon Secretion in a Glucose-Dependent Bidirectional Manner. Diabetes. 2019;68(1):34-44. doi: 10.2337/db18-0317
17. Lee YS, Jun HS. Anti-diabetic actions of glucagon-like peptide-1 on pancreatic beta-cells. Metabolism. 2014;63(1):9-19. doi: 10.1016/j.metabol.2013.09.010
18. Yang Y, Yu X, Huang L, Yu C. GLP-1R agonist may activate pancreatic stellate cells to induce rat pancreatic tissue lesion. Pancreatology. 2013;13(5):498-501. doi: 10.1016/j.pan.2013.07.281
19. Roussel M, Mathieu J, Dalle S. Molecular mechanisms redirecting the GLP-1 receptor signalling profile in pancreatic β-cells during type 2 diabetes. Horm Mol Biol Clin Investig. 2016;26(2):87-95. doi: 10.1515/hmbci-2015-0071
20. Iwamoto Y, Kimura T, Dan K, Iwamoto H, Sanada J, Fushimi Y, et al. Tirzepatide, a dual glucose-dependent insulinotropic polypeptide/glucagon-like peptide 1 receptor agonist, exhibits favourable effects on pancreatic β-cells and hepatic steatosis in obese type 2 diabetic db/db mice. Diabetes Obes Metab. 2024;26(12):5982-94. doi: 10.1111/dom.15972
21. Marso SP, Bain SC, Consoli A, Eliaschewitz FG, Jódar E, Leiter LA, et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2016;375(19):1834-44. doi: 10.1056/NEJMoa1607141
22. Gerstein HC, Colhoun HM, Dagenais GR, Diaz R, Lakshmanan M, Pais P, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. Lancet. 2019;394(10193):121-30. doi: 10.1016/s0140-6736(19)31149-3
23. Blundell J, Finlayson G, Axelsen M, Flint A, Gibbons C, Kvist T, et al. Effects of once-weekly semaglutide on appetite, energy intake, control of eating, food preference and body weight in subjects with obesity. Diabetes Obes Metab. 2017;19(9):1242-51. doi: 10.1111/dom.12932
24. Sattar N, Lee MMY, Kristensen SL, Branch KRH, Del Prato S, Khurmi NS, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials. Lancet Diabetes Endocrinol. 2021;9(10):653-62. doi: 10.1016/s2213-8587(21)00203-5
25. Frias JP, Nauck MA, Van J, Kutner ME, Cui X, Benson C, et al. Efficacy and safety of LY3298176, a novel dual GIP and GLP-1 receptor agonist, in patients with type 2 diabetes: a randomised, placebo-controlled and active comparator-controlled phase 2 trial. Lancet. 2018;392(10160):2180-93. doi: 10.1016/s0140-6736(18)32260-8
26. Heuvelman VD, Van Raalte DH, Smits MM. Cardiovascular effects of glucagon-like peptide 1 receptor agonists: from mechanistic studies in humans to clinical outcomes. Cardiovasc Res. 2020;116(5):916-30. doi: 10.1093/cvr/cvz323
27. Kristensen SL, Rørth R, Jhund PS, Docherty KF, Sattar N, Preiss D, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet Diabetes Endocrinol. 2019;7(10):776-85. doi: 10.1016/s2213-8587(19)30249-9
28. Liu L, Chen J, Wang L, Chen C, Chen L. Association between different GLP-1 receptor agonists and gastrointestinal adverse reactions: A real-world disproportionality study based on FDA adverse event reporting system database. Front Endocrinol (Lausanne). 2022;13:1043789. doi: 10.3389/fendo.2022.1043789
29. Ismaiel A, Scarlata GGM, Boitos I, Leucuta DC, Popa SL, Al Srouji N, et al. Gastrointestinal adverse events associated with GLP-1 RA in non-diabetic patients with overweight or obesity: a systematic review and network meta-analysis. Int J Obes (Lond). 2025;49(10):1946-57. doi: 10.1038/s41366-

025-01859-6
30. Bettge K, Kahle M, Abd El Aziz MS, Meier JJ, Nauck MA. Occurrence of nausea, vomiting and diarrhoea reported as adverse events in clinical trials studying glucagon-like peptide-1 receptor agonists: A systematic analysis of published clinical trials. Diabetes Obes Metab. 2017;19(3):336-47. doi: 10.1111/dom.12824
31. Ismail A, Amer MS, Tawheed A. Glucagon-like peptide-1 receptor agonists: evolution, gastrointestinal adverse effects, and future directions. World J Gastrointest Pharmacol Ther. 2025;16(3):107148. doi: 10.4292/wjgpt.v16.i3.107148
32. Ismail A, Amer MS, Tawheed A. Glucagon-like peptide-1 receptor agonists: evolution, gastrointestinal adverse effects, and future directions. World J Gastrointest Pharmacol Ther. 2025;16(3):107148. doi: 10.4292/wjgpt.v16.i3.107148
33. Kushner RF, Almandoz JP, Rubino DM. Managing Adverse Effects of Incretin-Based Medications for Obesity. Jama. 2025;334(9):822-3. doi: 10.1001/jama.2025.11153
34. He L, Wang J, Ping F, Yang N, Huang J, Li W, et al. Dipeptidyl peptidase-4 inhibitors and gallbladder or biliary disease in type 2 diabetes: systematic review and pairwise and network meta-analysis of randomised controlled trials. Bmj. 2022;377:e068882. doi: 10.1136/bmj-2021-068882
35. Zeng Q, Xu J, Mu X, Shi Y, Fan H, Li S. Safety issues of tirzepatide (pancreatitis and gallbladder or biliary disease) in type 2 diabetes and obesity: a systematic review and meta-analysis. Front Endocrinol (Lausanne). 2023;14:1214334. doi: 10.3389/fendo.2023.1214334
36. Gong J, Gao F, Jiang K, Xie Q, Zhao X, Lei Z. Risk of biliary diseases in patients with type 2 diabetes or obesity treated with tirzepatide: A meta-analysis. J Diabetes Investig. 2025;16(1):83-92. doi: 10.1111/jdi.14340
37. Li L, Shen J, Bala MM, Busse JW, Ebrahim S, Vandvik PO, et al. Incretin treatment and risk of pancreatitis in patients with type 2 diabetes mellitus: systematic review and meta-analysis of randomised and non-randomised studies. Bmj. 2014;348:g2366. doi: 10.1136/bmj.g2366
38. Monami M, Dicembrini I, Nardini C, Fiordelli I, Mannucci E. Glucagon-like peptide-1 receptor agonists and pancreatitis: a meta-analysis of randomized clinical trials. Diabetes Res Clin Pract. 2014;103(2):269-75. doi: 10.1016/j.diabres.2014.01.010
39. Crisafulli S, Alkabbani W, Paik JM, Bykov K, Tavakkoli A, Glynn RJ, et al. Comparative Gastrointestinal Safety of Dulaglutide, Semaglutide, and Tirzepatide in Adults With Type 2 Diabetes. Ann Intern Med. 2026;179(1):1-11. doi: 10.7326/annals-25-01724
40. Deirmenjian JM, Dagher C. 6486 Gastroparesis Exacerbation by a GLP-1 Agonist. Journal of the Endocrine Society. 2024;8(Supplement_1):bvae163.780. doi: 10.1210/jendso/bvae163.780
41. Bellavance D, Chua S, Mashimo H. Gastrointestinal Motility Effects of GLP-1 Receptor Agonists. Curr Gastroenterol Rep. 2025;27(1):49. doi: 10.1007/s11894-025-00995-3
42. Kelly CA, Sipos JA. Approach to the Patient With Thyroid Nodules: Considering GLP-1 Receptor Agonists. J Clin Endocrinol Metab. 2025;110(6):e2080-e7. doi: 10.1210/clinem/dgae722
43. Hu W, Song R, Cheng R, Liu C, Guo R, Tang W, et al. Use of GLP-1 Receptor Agonists and Occurrence of Thyroid Disorders: a Meta-Analysis of Randomized Controlled Trials. Front Endocrinol (Lausanne). 2022;13:927859. doi: 10.3389/fendo.2022.927859
44. Bezin J, Gouverneur A, Pénichon M, Mathieu C, Garrel R, Hillaire-Buys D, et al. GLP-1 Receptor Agonists and the Risk of Thyroid Cancer. Diabetes Care. 2023;46(2):384-90. doi: 10.2337/dc22-1148