**QUALITY IN SPORT**
*eISSN 2450-3118 · Open Access · Peer-reviewed*
apcz.umk.pl/QS Nicolaus Copernicus University in Toruń



**DRÓŻDŻ, Michał Antoni, MARCAK, Maria, NOWICKA, Weronika, KOŻUCH, Anna and RYMARCZYK, Emilia. Use of GLP-1 receptor agonists and dual agonists in patients with inflammatory bowel disease. Quality in Sport. 2026;77:76265. https://doi.org/10.12775/QS.2026.77.76265**

**ARTICLE TIMELINE**
**Received: 25.09.2026. Accepted: 01.10.2026. Published: 02.10.2026.**

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal 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 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 2026.

OPEN ACCESS · CC BY-NC-SA 4.0 This article is published with open access under the License Open Journal Systems of Nicolaus Copernicus University in Toruń, Poland, and is distributed under the terms of the Creative Commons Attribution Non-commercial Share Alike License (http://creativecommons.org/licenses/by-nc-sa/4.0/), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the work is properly cited. The authors declare no conflict of interest regarding the publication of this paper.

# Use of GLP-1 receptor agonists and dual agonists in patients with inflammatory bowel disease

Authors:

**Michał Dróżdż [MD]**

ORCID https://orcid.org/0009-0004-8933-0299

drozdz.m.29@gmail.com

Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland

**Maria Marcak [MM]**

ORCID https://orcid.org/0009-0005-2810-798X

marysiamarcak@gmail.com

Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland

**Weronika Nowicka [WN]**

ORCID https://orcid.org/0009-0002-4555-3189

wronkanowicka@gmail.com

Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland

**Anna Kożuch [AK]**
ORCID https://orcid.org/0009-0000-6315-6895
anna.kozuch02@gmail.com
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland

**Emilia Rymarczyk [ER]**
ORCID https://orcid.org/0009-0009-2172-6429
em.rymarczyk@gmail.com
Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland

Coresponding Author
**Maria Marcak**, e-mail: marysiamarcak@gmail.com

**Abstract**

**Background:** Obesity represents a growing epidemiological problem in patients with inflammatory bowel disease (IBD), affecting up to 40% of patients. Excess adipose tissue worsens clinical prognosis, sustains systemic inflammation, and accelerates the loss of response to biological therapy.

**Aim:** The aim of this study was to summarize current knowledge regarding the use of glucagon-like peptide-1 receptor agonists (GLP-1RAs) and dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonists (tirzepatide) in this patient group.

**Materials and methods:** PubMed Scopus, Web of Science, and Cochrane Library databases were searched from their inception through September 2026 using a combination of relevant keywords. A total of 20 studies were included in the review.

**Results:** Incretin-based therapies demonstrate immunomodulatory and intestinal barrier–protective effects. Real-world studies and meta-analyses show that semaglutide, liraglutide, and tirzepatide induce significant weight loss (6–12%+), reduce C-reactive protein levels, hospitalization rates, corticosteroid use, and the risk of IBD-related surgery by up to 55%. These agents are generally well tolerated and are not associated with an increased risk of IBD exacerbations. Delayed gastric emptying remains an important consideration, particularly in patients receiving oral thiopurines due to the potential for altered drug pharmacokinetics and hepatotoxicity.

**Conclusions:** GLP-1 and GIP/GLP-1 agonists represent a highly promising, safe adjunctive therapy for patients with IBD and metabolic disorders. Results from ongoing randomized controlled trials will allow for the definitive establishment of their position in gastroenterological guidelines.
**Keywords:** Inflammatory Bowel Disease, GLP-1 Receptor Agonists, Obesity, Tirzepatide, Mucosal Healing

## 1. Introduction

Inflammatory Bowel Diseases (IBD) represent a group of chronic, relapsing autoimmune disorders of the gastrointestinal tract, leading to progressive damage to the intestinal mucosa and wall. The two main disease entities comprising IBD are ulcerative colitis (UC) and Crohn's disease (CD). UC is characterized by continuous, superficial inflammation limited to the mucosal and submucosal layers of the large intestine, starting from the rectum and involving a variable length of the colon. CD is characterized by transmural (full-thickness) inflammation that can affect any segment of the gastrointestinal tract, from the mouth to the anus, and frequently leads to structural complications such as strictures, fistulas, or abscesses. Despite the introduction of modern therapies, aminosalicylates (5-ASA), glucocorticoids, immunomodulatory drugs (thiopurines), as well as targeted biological agents (TNF-α inhibitors, anti-IL-12/23, anti-integrins), and small molecules (JAK inhibitors) the proportion of patients failing to achieve sustained remission remains high. It is estimated that 40% to 60% of patients exhibit a primary or secondary loss of response to advanced biological treatment. This stems from the heterogeneity of inflammatory pathomechanisms, increasing drug immunogenicity, and the overlap of systemic metabolic disorders [1-3]

Historically, IBD was viewed as a condition predominantly associated with wasting, malnutrition, and weight loss. However, contemporary epidemiological data indicate that obesity (BMI ≥30 kg/m²) affects 15%–40% of adults with IBD, while an additional 20%–40% are overweight [2-6]. The coexistence of obesity and IBD creates a vicious immunometabolic cycle in which excess adiposity promotes systemic and intestinal inflammation, while chronic inflammation may further contribute to metabolic dysfunction [3,7]. Excess adipose tissue, particularly visceral and mesenteric adipose tissue (so-called “creeping fat”), acts as an active endocrine and immunological organ, producing a range of pro-inflammatory adipokines and cytokines, including TNF-α, IL-

6, and leptin, thereby sustaining chronic, low-grade systemic inflammation [2,3,6]. In addition, excess body mass may alter the pharmacokinetics of biological therapies by increasing the volume of distribution and systemic clearance of monoclonal antibodies such as infliximab and adalimumab [2,5,8,9]. Consequently, obese patients may exhibit lower serum trough drug concentrations, potentially contributing to accelerated loss of therapeutic response and shorter periods of disease control [3,5,10]. Importantly, obesity in patients with IBD has also been associated with a higher risk of hospitalization, increased corticosteroid requirements, higher rates of surgical complications, and a lower likelihood of achieving clinical and endoscopic remission. Collectively, these mechanisms underscore the complex interplay between adiposity, inflammation, treatment response, and clinical outcomes in patients with IBD [2,3,5,11].

The utilization of incretin hormone receptors has become a breakthrough in the treatment of metabolic disorders. Endogenous GLP-1 is a peptide released by enteroendocrine L cells of the small and large intestine in response to food ingestion [4,6,12,13], as well as under conditions of intestinal barrier damage via the stimulation of TLR4 receptors by lipopolysaccharide (LPS) [8,13,14].

## 2. Classical Incretin and Metabolic Actions

### 2.1. Regulation of Glucose Homeostasis and Control of Appetite and Body Mass

GLP-1 stimulates glucose-dependent insulin secretion by pancreatic β-cells and inhibits glucagon secretion by α-cells [4,6,12]. Through the activation of central pathways in the hypothalamus as well as delaying gastric emptying and slowing intestinal transit, drugs in this class induce a feeling of satiety, significantly reducing caloric intake [2,4,6,8,12].

### 2.2. Direct and Indirect Immunomodulatory Actions

GLP-1R receptors are expressed not only in the pancreas and nervous system, but also on intestinal epithelial cells and immune cells (macrophages, monocytes, T lymphocytes, intraepithelial T lymphocytes [IELs], and group 3 innate lymphoid cells [ILC3s]) [4,8,12,14]. GLP-1R activation triggers multidirectional anti-inflammatory cascades [1,12].

GLP-1R signaling increases cAMP levels and activates PKA kinase, which inhibits the nuclear translocation of the NF-κB p65 factor and dephosphorylates AKT, ERK1/2, JNK, and p38 MAPK kinases [8,12,13]. This leads to a significant reduction in the synthesis of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, COX-2) [1,3,12].

GLP-1R stimulation promotes a macrophage phenotype switch from pro-inflammatory M1 to antiinflammatory/reparative M2 (dependent on the cAMP/PKA/STAT3 pathway) [8], supports regulatory T lymphocyte (Treg) differentiation via TGF-β [3,8], and drives the expansion of IL-22- producing ILC3 cells [3,8].

GLP-1 analogs increase the expression of tight junction proteins (ZO-1, occludin, claudin-1) [1,13], enhance mucin production (MUC5B) and protective secretion in Brunner's glands [8,12], and induce autophagy in the colon, preventing Paneth cell dysfunction and metaplasia [15].

Therapy favors the restoration of gut microbiome diversity (including an increased abundance of Lactobacillaceae, Bifidobacteriaceae, Akkermansia) [5,8,13].

## 3. Characteristics of Individual Drugs

### 3.1. Liraglutide

A GLP-1 analog administered subcutaneously once daily (at doses up to 1.8 mg in type 2 diabetes (T2D) and 3.0 mg in obesity under the brand name Saxenda)[12]. Well-studied in preclinical colitis models; strongly induces colonic autophagy and protects the intestinal barrier in duodenal Brunner's glands [1,13,15].

### 3.2. Semaglutide

A long-acting analog administered subcutaneously once weekly (Ozempic, Wegovy) or in oral form [7,12]. Demonstrates the highest body weight reduction efficacy among pure GLP-1RAs (~15% in the general population, ~6–10% in IBD patients) [3,4,5]. In clinical and registry studies, it induces a significant reduction in CRP levels [9,10,12] and a 67% reduction in the risk of IBD-related surgical procedures (HR 0.33) [9].

### 3.3. Dulaglutide and Exenatide

Older generation GLP-1 agonists, primarily used in T2D [5,12]. Exenatide was one of the first drugs in which a direct decrease of pro-inflammatory cytokines was demonstrated in IELs [8].

### 3.4. Tirzepatide

First-in-class dual GIP and GLP-1 receptor agonist, administered subcutaneously once weekly (Mounjaro, Zepbound). GIP improves insulin sensitivity in subcutaneous adipose tissue and enhances lipid buffering. The synergistic action of GIP/GLP-1 provides the greatest reduction in body weight (>10–15% in IBD patients) [7,12]. However, tirzepatide induces a stronger, transient slowing of gastric emptying after the first dose, which can lead to significant pharmacokinetic interactions with oral drugs used in IBD [11,16].

## 4. The Gut-Metabolic Axis and Anti-inflammatory Mechanisms of GLP-1

Endogenous GLP-1 is a peptide hormone formed as a result of post-translational processing of proglucagon (encoded by the GCG gene). It is secreted by enteroendocrine L cells of the small and large intestines, concentrated particularly in the terminal ileum and colon, under the influence of ingested nutrients [8,12,14]. Interestingly, in situations where the integrity of the intestinal barrier is disrupted, L cells also exhibit the ability to directly sense bacterial endotoxin via TLR4 receptors, which stimulates GLP-1 secretion as an early alarm and repair signal. GLP-1 receptors (GLP-1R) belong to class B G-protein-coupled receptors (Gs), and their activation stimulates adenylate cyclase to produce cyclic AMP (cAMP) and activate protein kinase A (PKA) [8,14]. These receptors are expressed not only in pancreatic cells or the central nervous system, but also in intestinal smooth muscle myocytes, Brunner's gland cells, myenteric plexus neurons, and on the surface of numerous immune cells – including macrophages, monocytes, IELs, circulating T lymphocytes (CD4+ and CD8+), Tregs, and ILC3s [3,8,12].

## 4.1. Key Signaling Cascades and Cellular Anti-inflammatory Mechanisms

### 4.1.1. Inhibition of the NF-κB Pathway and the AKT and MAPK Axes

A key element of the immunomodulatory action of GLP-1 in the intestinal mucosa is the blockade of the nuclear transcription factor NF-κB. Activation of the cAMP/PKA axis prevents the phosphorylation and nuclear translocation of the NF-κB p65 subunit, which directly inhibits the gene transcription for pro-inflammatory cytokines, chemokines, and adhesion molecules (TNF-α, IL-1β, IL-6, COX-2, iNOS, CXCL1, IL-8) [8,12,13]. Concurrently, GLP-1RAs abolish the excessive phosphorylation of AKT kinase and MAPK family kinases: ERK1/2, JNK, and p38 MAPK, suppressing the inflammatory response stimulated by pathogen-associated factors [13].

### 4.1.2. Macrophage Repolarization and Modification of the T-Cell Profile.

GLP-1RAs inhibit the polarization of macrophages toward the pro-inflammatory M1 phenotype while promoting their transition into the reparative M2 phenotype. This mechanism relies on 5. cAMP/PKA induction, inhibition of JNK phosphorylation, and activation of the transcription factor STAT3 [8].

GLP-1R stimulation in the IEL population limits TCR-dependent signaling via the blockade of ZAP-70 kinase and the SLP-76 protein. This leads to a strong suppression of Th1 and Th17 cytokine release, such as IFN-γ, IL-2, IL-17A, IL-4, IL-5, and TNF-α [8].

GLP-1R signaling increases TGF-β production, driving the differentiation of immunomodulatory Tregs producing IL-10 [3,8,12]. Additionally, it activates ILC3s, which secrete IL-22 – a key cytokine responsible for intestinal epithelial regeneration and homeostasis [3,15].

### 4.1.3. Enhancement of Intestinal Barrier Integrity and Function

GLP-1RAs directly restore the expression of tight junction proteins, such as ZO-1, occludin, and claudin-1, which are lost during the inflammatory process [1,13]. Furthermore, they stimulate mucin expression (MUC5B) in goblet cells, enhance secretion in duodenal

Brunner's glands, induce the expression of repair genes (Tff1, Tff2, Egfr, Fgf7, Hgf), and stimulate intestinal crypt growth and division (so-called crypt fission), protecting against their subacute atrophy [8,14].

#### 4.1.4. Induction of Autophagy and Protection of Paneth Cells

Impairments in the autophagy process (the cellular cleanup and recycling mechanism) are strongly linked to the pathogenesis of IBD (e.g., in patients with ATG16L1gene mutations). GLP-1RAs (particularly liraglutide) restore normal autophagic flux in colonic epithelial cells. This is manifested by increased formation of autophagosomes and autolysosomes, as well as the efficient degradation of the selective substrate p62 (SQSTM1). As a result, these drugs protect Paneth cells from cellular dysfunction and halt their abnormal metaplasia in the colon.

#### 4.1.5. Microbiome Modulation and Reduction of Oxidative Stress

GLP-1RAs attenuate the dysbiosis accompanying colitis, favoring the proliferation of health-promoting bacteria from the Lactobacillaceae and Bifidobacteriaceae families and the genus Akkermansia [5,15]. This is accompanied by activation of the AMPK pathway, an increase in short-chain fatty acid (SCFA) production, and the quenching of reactive oxygen species (ROS) [3,4,12,13].

## 5. Preclinical Data (In Vitro and Animal Model Studies)

Numerous preclinical studies utilizing cell cultures and animal models of experimental colitis provide evidence for the direct anti-inflammatory and regenerative actions of GLP-1 and its analogs [13,14,15].

### 5.1. In Vitro Studies

#### 5.1.1. LPS-Stimulated RAW264.7 Macrophages

In studies on the murine RAW264.7 macrophage line treated with LPS, administration of GLP-1 in a dose-dependent manner (10, 20, 50 μmol/L) significantly inhibited mRNA levels and protein expression of

the pro-inflammatory enzymes iNOS and COX-2 and cytokines TNF-α, IL-1β, and IL-6. Biochemical analyses demonstrate that this effect stems directly from the suppression of pAKT, p-NF-κB p65, and p-ERK1/2, p-JNK, and p-P38 MAPK kinase phosphorylation [13].

#### 5.1.2. Intraepithelial T Lymphocyte (IEL) Cultures

Ex vivo stimulation of anti-CD3/CD28 antibody-stimulated IELs showed that the GLP-1 analog exenatide significantly reduced the release of pro-inflammatory cytokines (IL-2, IL-17A, IFN-γ, TNF-α), which did not occur in mice with a T-cell-specific GLP-1 receptor knockout [13].

### 5.2. In Vivo Studies in Animal Models

#### 5.2.1. Dextran Sulfate Sodium (DSS)-Induced Colitis Model

In studies by Wang et al. (2023) and Saadoun et al. (2025), administration of GLP-1 or liraglutide (at doses of 0.2 and 0.6 mg/kg/day) to mice with induced acute colitis produced a clear, dosedependent reduction in the Disease Activity Index (DAI), lengthening of the inflammation-shortened colon, and inhibition of weight loss [8].

GLP-1 administration restored normal histological mucosa architecture, protected goblet cells from mucin depletion, limited neutrophil and macrophage infiltration, and stimulated ZO-1 and occludin synthesis. This was accompanied by a significant drop in myeloperoxidase (MPO) activity and TNF-α, IL-1β, and IL-6 concentrations in colonic tissue [13, 15].

The study by Saadoun et al. (2025) demonstrated that liraglutide significantly reduced excessive lysozyme expression in the colon and inhibited abnormal Paneth cell metaplasia in the distal large intestine. Electron microscopy (EM) analyses confirmed that liraglutide restored efficient autophagic flux (stimulated the formation of autophagosomes and autolysosomes as well as a decrease in p62). Importantly, following administration of chloroquine (an autophagosomelysosome fusion

blocker), p62 accumulated, confirming that the beneficial effect of liraglutide is mechanically linked to autophagy induction [13, 15].

#### 5.2.2. Adoptive T-Cell Transfer Model (CD4+CD45RBhigh in SCID Mice)

The long-acting analog liraglutide (0.6 mg/kg) administered over 35 days to SCID mice with Tcell transfer-induced colitis significantly attenuated inflammation, improved the colon weight-tolength ratio, lowered the histopathological score, and reduced pro-inflammatory cytokine levels through the upregulation of barrier genes (IL-33, CCL20, MUC5B) [15].

#### 5.2.3. GLP-1 Receptor Deficiency (GLP-1R KO)

Mice lacking the GLP-1R receptor (GLP-1R KO) subjected to 3% DSS exhibited a significantly more severe course of colitis than wild-type (WT) mice – accelerated weight loss, higher DAI score, extensive epithelial necrosis, and impaired transcription of protective genes (Tff3, Ifng, Tgfb2) were observed. Furthermore, germ-free GLP-1R knockout mice showed higher mortality due to colitis [8,14].

#### 5.2.4. Use of GLP-1 Nanocarriers (GLP-1-SSM)

Anbazhagan et al. utilized GLP-1 in combination with sterically stabilized phospholipid micelles (GLP-1-SSM), allowing for targeted, local delivery of the peptide to inflamed intestinal tissue. This therapy significantly reduced IL-1β expression, prevented the downregulation of the chloride anion transporter (DRA), and attenuated diarrhea in mice with colitis [2,14].

## 6. Clinical Evidence from Observational and Retrospective Studies

Due to the fact that patients with IBD were historically excluded from pivotal Phase 3 clinical trials for GLP-1 receptor agonists and dual GIP/GLP-1 agonists, abundant clinical evidence currently stems from population-based retrospective studies, large administrative databases, and meta-analyses published between 2021 and 2026 [4,8].

## 6.1. Metabolic Efficacy and Weight Loss in IBD Patients

Numerous retrospective cohort studies confirm that GLP-1RAs and dual agonists demonstrate high efficacy in weight reduction in patients with IBD and concomitant obesity, achieving results similar to the general population [4,5].

### 6.1.1. Semaglutide and Liraglutide

In a study by Ramos Belinchón et al. (2024), in IBD patients treated with semaglutide (1.0 mg) or liraglutide (3.0 mg), the median weight change after 6 months was -6.2% (-5.7 kg), and 58.3% of patients achieved a weight loss of ≥5% [2,17]. In a single-center study by St-Pierre, Klein et al. (2024), non-diabetic IBD patients with BMI ≥ 30 kg/m² using semaglutide or tirzepatide showed a significant reduction in median BMI from 34.0 to 31.0 kg/m² ($p < 0.0001$) and a median total body weight loss of 8.15 kg ($p < 0.0001$) after a median follow-up of 450 days [11]. Clarke et al. (2025) analyzed a cohort of 272 IBD patients, 175 of whom completed 12 months of GLP-1RA therapy. Mean weight loss was 8.72% (BMI change of -3.26 kg/m²), with 61% of patients achieving a weight loss of ≥5%, and 42% achieving a loss of ≥10%. Efficacy was highest for semaglutide (76% of patients with ≥5% loss) and liraglutide (58.8%) [5].

### 6.1.2. Tirzepatide

In a comprehensive TriNetX database study published by Desai et al. (2025), encompassing 274 IBD patients taking tirzepatide, a mean weight reduction of 21 lbs (~9.5 kg / >10% body weight) was demonstrated over a period of 6 to 15 months. Dose escalation of tirzepatide to 15 mg was associated with a mean weight drop of 29 lbs (~13.1 kg). Although this weight reduction was lower than that following bariatric surgery (-55 lbs, $p < 0.0001$), tirzepatide proved to be a potent and less invasive pharmacological alternative [7].

## 6.2. Impact on Hard Endpoints - Surgical Procedures, Hospitalizations, and Corticosteroid Therapy

Although the primary indication for GLP-1RA use was metabolic disorders, analysis of large national registries and multicenter databases points to significant benefits regarding the clinical course of IBD [4].

A meta-analysis comprising 6 retrospective cohort studies demonstrates that GLP-1RA use in patients with IBD and metabolic disorders is associated with a statistically significant 55% reduction in the risk of IBD-related surgical procedures (pooled RR = 0.45; 95% CI: 0.35–0.59; $I^2$ = 38.1%). Sensitivity analysis confirmed high stability and reproducibility of this result [1]. A study by Villumsen et al. including 3,751 patients with IBD and type 2 diabetes showed that patients using GLP-1 / DPP-4i-based therapies exhibited a significantly lower risk of the composite endpoint (corticosteroids, biologic treatment, hospitalizations, surgeries) compared to individuals taking other anti-diabetic drugs (adjusted IRR = 0.52; 95% CI: 0.42–0.65) [18]. Breakdown of individual endpoints shows a drop in the risk of requiring corticosteroid initiation (aIRR = 0.54; 95% CI: 0.41–0.70) and IBD-related hospitalizations (aIRR = 0.73; 95% CI: 0.58– 0.91) [4,18]. An analysis of 3,737 IBD patients by Gorelik et al. demonstrated that GLP-1 analog use was associated with a decreased risk of adverse intestinal events (HR = 0.79; 95% CI: 0.66– 0.96), with particularly pronounced benefits in patients with ulcerative colitis (HR = 0.73) and individuals with obesity (BMI ≥ 30 kg/m²) [4,8]. In a propensity score-matched (PSM) study including 562 patients with obesity and IBD, semaglutide use was associated with a significant 67% reduction in the risk of IBD-related surgical procedures (HR = 0.33; 95% CI: 0.13–0.83). Significantly, in the group of 89 patients taking tirzepatide, no patient required IBD-related surgery (compared to 2 cases in the control group) [9]. Desai et al., in an analysis of 274 IBD patients taking tirzepatide, a significantly lower risk of all-cause hospitalization was demonstrated compared to the control group (aOR = 0.48; 95% CI: 0.35–0.66; $p < 0.0001$) [7].

### 6.3. Inflammatory Markers (CRP, Fecal Calprotectin) and Clinical and Endoscopic Activity

#### 6.3.1. C-Reactive Protein (CRP)

A decrease in serum CRP concentration is one of the most consistent findings in clinical studies [4]. Anderson et al. (2025) observed a drop in mean CRP concentration from 12.92 mg/dL to 6.38 mg/dL ($p = 0.005$) after 1 year of GLP-1RA use, with no correlation with the degree of weight loss [10]. In the OneFlorida+ study (2025), patients using GLP-1 displayed a median CRP reduction of -0.3 mg/L, whereas an increase of +0.8 mg/L was recorded in the control group ($p = 0.02$) [9].

#### 6.3.2. Fecal Calprotectin (FCP)

Studies evaluating the specific marker of intestinal inflammation, fecal calprotectin, showed a trend toward a decrease or stabilization of its median concentration (e.g., in the study by Ramos Belinchón, a drop from 40.9 µg/g to 32.7 µg/g, $p = 0.376$) [2,3,4].

#### 6.3.3. Clinical and Endoscopic Indices

Cohort studies recorded no negative impact on disease activity indices (Harvey-Bradshaw Index [HBI] for CD, Mayo score for UC) [2,4,10]. Case reports (including Klein et al., ac9-13-e02070) document isolated cases of achieving complete clinical, endoscopic, and histological remission in patients with refractory UC following the initiation of semaglutide [19].

## 7. Safety, Tolerability, and Clinical Pitfalls

### 7.1. Gastrointestinal Adverse Events and Discontinuation Rates

The safety profile of GLP-1RA drugs in IBD patients is fully consistent with that observed in the general population, although gastrointestinal complaints represent the primary limitation to tolerability [3,4]. Symptom Incidence included nausea (11% to 31%), constipation (11% to 25%) [4,5,11], diarrhea

(2.2% to 12.5%) [2,4,5], vomiting and abdominal pain (1.1% to 14.6%) [4,10,11]. In real-world clinical practice, treatment discontinuation of GLP-1RAs affects 11% to 24% of IBD patients, with nearly half (48%) resulting from gastrointestinal intolerance, and the remainder from financial constraints or loss of drug access [3,5]. Analyses indicate that tirzepatide was characterized by the best overall tolerability (16% adverse events) compared to semaglutide (47%) [5].

### 7.2. Differentiating Adverse Symptoms from IBD Flare

One of the greatest challenges in gastroenterological practice is the overlap of GLP-1RA adverse symptoms (nausea, altered bowel habits, abdominal cramps) with IBD flare symptoms. Misinterpreting drug-induced nausea or diarrhea as a disease flare can lead to unwarranted escalation of immunosuppressive treatment or unnecessary corticosteroid therapy [3,4,6]. Comprehensive cohort studies (Clarke et al., 2025; Levine et al., 2025) demonstrated no increase in the incidence of IBD flares within 12 months following GLP-1RA initiation (13% postGLP-1 vs 17% pre-GLP-1; $p = 0.40$) [5,6].

### 7.3. Safety regarding Intestinal Obstruction (Ileus) and Pancreatitis

Due to the slowing of intestinal transit, there were concerns that patients with the stricturing phenotype of CD might be at risk for obstruction [4,17]. However, the Danish Nationwide Cohort Study (Nielsen et al., 2025) comprising 61,927 IBD patients unambiguously demonstrated that GLP-1RA use was not associated with an increased risk of intestinal obstruction (HR = 0.57; 95% CI: 0.36–0.88) [3,4]. Similar conclusions were drawn by Weng et al. (2025) [6]. In cohorts of IBD patients, the incidence of pancreatitis during GLP-1RA therapy ranged from 0.57% to 2.4% and did not differ from the control group (HR = 0.74; 95% CI: 0.37–1.47) [4,9,10].

### 7.4. Pharmacokinetic Interactions – The Case of Thiopurine Toxicity (6-MP / Azathioprine) and Biologics

In a clinical report by Klein et al. describing a 42-year-old female patient with UC status-post colectomy with J-pouch creation, who was in durable remission on 6-mercaptopurine (6-MP) monotherapy, initiation of tirzepatide (7.5 mg)

induced a weight loss of 14.1 kg, but led to a rapid elevation of liver enzymes (ALT 75 U/L) and a toxic spike in thiopurine metabolite concentrations. 6-TG increased from levels of 209–281 pmol to 512 pmol/8×108 RBC, 6-MMP increased from levels of 3,711–3,932 pmol to a toxic value of 11,704 pmol/8×108 RBC [16]. The action of tirzepatide in delaying gastric and duodenal emptying significantly prolonged the absorption time of oral 6-MP, increasing its bioavailability [8,16]. Additionally, the loss of body mass altered the mass-based drug dose per kg. Following a reduction in the 6-MP dose, liver enzyme levels normalized [11,16]. Substantial loss of adipose tissue in patients receiving monoclonal antibodies (anti-TNF, anti-IL-23) may lower drug clearance and volume of distribution, which theoretically raises serum trough levels and may require dose adjustment of biological treatment [8].

### 7.5. Changes in Body Composition (Sarcopenia) and Challenges in Endoscopic Procedures (Bowel Preparation)

Sarcopenia (loss of muscle mass and strength) affects up to 52% of patients with CD and 37% with UC. Because weight loss induced by GLP-1RAs encompasses both fat mass and lean muscle mass, elderly or debilitated patients face a risk of exacerbated sarcopenia. Adequate protein intake and resistance training are recommended. Delayed gastric emptying caused by GLP-1RAs may decrease the efficacy of oral bowel cleansing preparations prior to colonoscopy and increase the risk of gastric content aspiration during gastroscopy under anesthesia. Adopting a clear liquid diet 24 hours before the procedure or temporary withholding of the drug dose is recommended. Slowing of gastric absorption may decrease the efficacy of oral contraceptive pills, which requires patient education and consideration of alternative methods [8].

## 8. Drug Comparison

### 8.1. Metabolic Efficacy (Weight Reduction)

Among the drugs in this class, semaglutide and tirzepatide demonstrate higher efficacy in reducing body weight and BMI in IBD patients compared to liraglutide [2,5,7]. Tirzepatide, through its dual action on GIP and GLP-1 receptors, allows for a dose-dependent weight loss exceeding 10–12% [7].

### 8.2. Disease-Modifying Effect in IBD

Semaglutide currently holds the strongest support in database analyses regarding a direct reduction in the risk of surgical procedures in patients with Crohn's disease (HR = 0.33) [9] and documented improvement in endoscopic and histological intestinal parameters [19]. Liraglutide has the most thoroughly explored preclinical mechanism – studies in mouse models of colitis demonstrate its unique ability to stimulate colonic autophagy and prevent damage to intestinal crypts [15].

### 8.3. Pitfalls and Pharmacological Interactions

Particular caution must be exercised when using tirzepatide (and other potent agonists) in patients taking oral immunomodulators, especially thiopurines (azathioprine, 6-mercaptopurine) [8,19]. Significant slowing of gastric and duodenal emptying caused by tirzepatide can lead to a rapid accumulation of toxic metabolites (6-TG and 6-MMP), resulting in liver injury. In these patients, recommending serum metabolite concentration monitoring after initiating therapy is essential [8,19].

*Table 1. Comparative characteristics of liraglutide, semaglutide, and tirzepatide in patients with inflammatory bowel disease*

| **Feature / Parameter** | **Liraglutide (Saxenda, Victoza)** | **Semaglutide (Ozempic, Wegovy)** | **Tirzepatide (Mounjaro, Zepbound)** |
|---|---|---|---|
| **Pharmacological class** | Selective glucagon-like peptide-1 receptor agonist (GLP-1RA); short- to intermediate-acting analogue [8,15]. | Long-acting selective GLP-1 receptor agonist (GLP-1RA) [8,11]. | Dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist [11,16]. |

| | | | |
|---|---|---|---|
| **Dosing regimen** | Subcutaneous administration once a day, with dose titration from 0.6 mg to 3.0 mg/day [2,15]. | Subcutaneous administration once a week, with dose titration from 0.25 mg to 1.0–2.4 mg/week [2,19]. | Subcutaneous administration once a week, with dose titration from 2.5 mg to 10–15 mg/week [7]. |
| **Mean weight reduction in patients with IBD** | Approximately 1.8%–6.6% (or 1.8–5.7 kg) over 6–12 months [2,17]. Approximately 58.8% of patients achieve ≥5% weight loss [5]. | Approximately 5.4%–9.8% (or 6.2–8.1 kg / 16 lb) over 6–12 months [2,11]. Up to 76% of patients achieve ≥5% weight loss [5]. | Dose-dependent weight reduction of approximately 7% to >10%–12% (mean approximately 21 lb / 9.5 kg; up to 29 lb / approximately 13 kg with a 15-mg dose) [7]. |
| **Effects on IBD activity and inflammatory markers** | Reduction in inflammatory activity in preclinical models. A case of marked clinical remission has also been reported [15]. | Significant reduction in C-reactive protein (CRP) levels [9,10] and a 67% reduction in the risk of IBD-related surgery (HR 0.33) [9]. Endoscopic and histological remission has been reported in case reports [19]. | Reduction in the risk of overall hospitalization (OR 0.48) and a numerical reduction in CRP levels [4,7]. A very low rate of IBD-related surgery has been reported [9]. |
| **Gastrointestinal tolerability profile** | Nausea is relatively common (12.5%–13.3%), with diarrhea also reported [2]. The need for daily injections may | Nausea (11%–31%), constipation (25%), and vomiting [11]. Overall gastrointestinal tolerability may be more favorable than that of | Gastrointestinal adverse effects are broadly comparable to those observed with semaglutide, |

| | | | |
|---|---|---|---|
| | affect treatment adherence. | shorter-acting GLP-1RAs [8]. | including nausea and constipation [11,20]. |
| **Risk of IBD flares** | No increased risk of IBD exacerbations has been reported [2,5]. | No increased risk of IBD exacerbations; associated with reduced rates of hospitalization and corticosteroid use [2,5,18]. | No increased risk of IBD exacerbations has been reported [5,7]. |
| **Key considerations and drug interactions** | Induction of autophagy in intestinal tissue and protection against Paneth cell metaplasia have been demonstrated in preclinical studies [15]. | Associated with reduced requirements for biologic therapy and systemic corticosteroids in population-based datasets [2,18]. | Potentially clinically significant interaction with thiopurines (6-mercaptopurine and azathioprine). Delayed gastric emptying may increase exposure to hepatotoxic metabolites by 2- to 3-fold [19]. |

## 9. Future Perspectives and Ongoing Clinical Trials (RCTs)

Future perspectives on the use of GLP-1 receptor agonists and multi-receptor agonists in IBD rely on transitioning from retrospective observations to controlled prospective trials, as well as on the development of new molecules and drug delivery technologies [1,8].

## 9.1. Ongoing and Planned Prospective Clinical Trials (RCTs)

A key step in verifying the direct impact of these drugs on the course of IBD is multicenter Phase 3b double-blind trials [8].

### 9.1.1. NCT06937086

A study evaluating the efficacy and safety of combining the biologic mirikizumab (an anti-IL-23 antibody) with tirzepatide (a dual GIP/GLP-1 agonist) compared to mirikizumab with placebo in patients with moderately to severely active UC and concomitant obesity or overweight. The primary goal is to evaluate whether simultaneous metabolic control and IL-23 blockade facilitates achieving symptomatic remission and a body weight reduction of at least 10% [8].

### 9.1.2. NCT06937099

An analogous prospective Phase 3b clinical trial evaluating the combination of mirikizumab with tirzepatide in adult patients with active CD and obesity [8].

### 9.1.3. NCT06774079

A study investigating tirzepatide as an adjunctive therapy in patients with CD and BMI > 27 kg/m² treated with TNF-α inhibitors (infliximab or adalimumab), also incorporating dietary interventions and assessment of inflammatory biomarkers [8].

## 9.2. Next-Generation Drugs and Multi-Receptor Agonists

Research on novel incretin molecules opens additional therapeutic avenues. Triple GIP/GLP-1/ Glucagon Agonists (retatrutide) and antibody-conjugated molecules modifying GIP signaling (maridebart cafraglutide / MariTide) provide even stronger body weight reduction and improvement in metabolic parameters. Combinations with Amylin Analogs (CagriSema) or amycretin demonstrate potential in multi-target appetite inhibition and body composition modification. Oral Small-Molecule GLP-1R Agonists (orforglipron) allow for convenient once-daily pill administration, facilitating chronic therapy in patients avoiding injections [8,20]. Dual GLP-1/ GLP-2 Agonists display

unique reparative effects, combining the immunomodulatory properties of GLP-1 with the potent trophic action of GLP-2 on the intestinal epithelium (stimulating mucosal healing and crypt regeneration) [8,14].

### 9.3. Targeted Intestinal Carriers and Nanotechnology

To minimize systemic gastrointestinal adverse effects while increasing drug concentration in inflamed tissue, work is underway on nanotechnological carriers (GLP-1-SSM phospholipid micelles or biodegradable PLGA nanoparticles). This technology enables targeted, local release of the peptide directly in the colon [1,13].

### 9.4. Unmet Research Needs and New Endpoints

Future prospective trials must focus on objective remission markers, such as endoscopic mucosal healing, histological indices, fecal calprotectin levels, and changes in microbiome composition. Equally critical will be the precise monitoring of body composition and lean muscle mass to prevent exacerbating sarcopenia in IBD patients, as well as evaluating clinical synergy when used concurrently with modern biologics and JAK inhibitors [1,4,8].

## 10. Summary

Obesity is a disease characterized by an excessive accumulation of adipose tissue. It currently affects 15% to 40% of adult patients with IBD, and an additional 20% to 40% struggle with being overweight [2,5,6]. Excess adipose tissue, particularly mesenteric and visceral adipose tissue, functions as an active secretory organ, releasing pro-inflammatory cytokines (including TNF-α, IL-6) and adipokines [2,3,19]. This state exacerbates the systemic inflammatory response, is associated with greater intensity of abdominal pain complaints, and adversely modifies the pharmacokinetics of biologic drugs by increasing their plasma clearance and volume of distribution [2,5,10].

Endogenous GLP-1 peptide is secreted by intestinal L cells, which, under conditions of mucosal damage, can directly sense bacterial endotoxin via TLR4 receptors. GLP-1R receptors are expressed on intestinal epithelial cells and immune cells, including macrophages, T lymphocytes, IELs, and ILC3s[8,12,13,19]. Administration of GLP-1 analogs triggers the following protective cascades .

GLP-1 analogs inhibit phosphorylation and nuclear translocation of the NF-κB p65 subunit and quench AKT and MAPK kinase cascades (p38, ERK1/2, JNK), which significantly reduces the synthesis of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, iNOS, COX-2) [3,12,13]. This therapy restores the expression of tight junction proteins (ZO-1, occludin, claudin-1) and mucin production (MUC5B). Furthermore, liraglutide stimulates colonic autophagy (via autophagosome formation and p62/SQSTM1 degradation), preventing abnormal Paneth cell metaplasia in the colon [1,13,15].

Treatment promotes a macrophage phenotype switch from pro-inflammatory M1 to reparative M2 (dependent on the cAMP/PKA/STAT3 axis), supports the differentiation of IL-10-secreting Tregs, and stimulates IL-22-producing ILC3 cells [3,8,19].

Meta-analysis of cohort studies confirmed that GLP-1RA use is associated with a statistically significant 55% reduction in the risk of IBD-related surgical procedures (pooled RR = 0.45; 95% CI: 0.35–0.59) [1]. In database analyses, semaglutide reduced the risk of intestinal surgeries in patients with obesity and IBD (HR = 0.33; 95% CI: 0.13–0.83) [9]. A decrease in IBD-related hospitalization rates and a reduced need for glucocorticosteroids were also demonstrated [4,18]. Beside mucosal healing, use of semaglutide or liraglutide provides a median weight loss of 6% to 10% (with the proportion of patients achieving ≥5% weight loss reaching 58%–76%) [2,3,4,5]. The dual agonist tirzepatide induces an even stronger weight reduction, exceeding 10%–12% [4,7]. GLP-1RA use is also associated with a statistically significant drop in serum CRP concentration [9,10]. Adverse events of GLP-1RA class drugs primarily concern the gastrointestinal tract (nausea 11%– 31%, constipation 11%–25%, diarrhea 2%–12%) and are transient in nature. Population studies confirm that GLP-1RA do not increase the risk of IBD flares or intestinal obstruction [4,5,6]. However, delayed gastric emptying may lead to elevated drug metabolite concentrations and subsequent transient liver injury; therefore, therapeutic drug monitoring for potentially toxic medications is strongly advised.[11,16,19].

GLP-1 receptor agonists and dual (GIP/GLP-1) agonists represent a highly valuable, safe, and effective adjunctive treatment option for patients with IBD and metabolic disorders. They combine efficient metabolic control with immunomodulatory action, intestinal mucosal reinforcement, and a clear reduction in surgical complications [1,4,8]. Ongoing prospective RCTs will refine their position in treatment guidelines for inflammatory bowel diseases [5,8].

Disclossure

Author Contributions

Conceptualization: [MD], [MM]

Methodology: [AK], [MM], [WN]

Check: [AK], [WN], [MM]

Investigation: [MD], [MM]

Data curation: [MD], [AK], [WN], [ER]

Writing -rough preparation: [MD]

Writing -review and editing: [MD], [MM]

Visualization: [AK], [MD], [WN]

Project administration: [MM], [AK]

Funding

The article did not receive any funding

Institutional Review Board Statement

Not Applicable.

Informed Consent Statement

Not Applicable.

Data Availability Statement

Not Applicable.

Acknowledgements

This research has not received any administrative or technical support.

Conflicts of Interest

The authors declare no conflict of interest.

All authors have read and agreed with the published version of the manuscript.

Declaration of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the author used ChatGPT (OpenAI) for language editing, improving readability and clarity of the text, and assistance with grammar and style. The author carefully reviewed and edited all AI-generated suggestions and takes full responsibility for the accuracy, originality, and scientific content of the manuscript.

.

Bibliography


1. Yang, M., Huo, Y., Liu, Z., Bai, G., He, D., & Zhang, L. (2025). The role of GLP-1 receptor agonists in IBD-related surgery and IBD-related complications of inflammatory bowel disease among patients with metabolic comorbidities: a systematic review and meta-analysis. Frontiers in medicine, 12, 1621958. https://doi.org/10.3389/fmed.2025.1621958
2. Ramos Belinchón, C., Martínez-Lozano, H., Serrano Moreno, C., Hernández Castillo, D., Lois Chicharro, P., Ferreira Ocampo, P., Marín-Jiménez, I., Bretón Lesmes, I., & Menchén, L. (2024). Effectiveness and safety of a GLP-1 agonist in obese patients with inflammatory bowel disease. Revista espanola de enfermedades digestivas, 116(9), 478–483. https://doi.org/10.17235/reed.2024.10305/2024
3. Fernando, S., Zhao, J., Josloff, K., Zubair, N., Desai, A., Shivashankar, R., Kozuch, P. L., Choudhary, C., Lichtenstein, G., & Sehgal, P. (2026). Glucagon like peptide 1 receptor agonists in patients with inflammatory bowel disease: safety, clinical effectiveness and anti-inflammatory mechanisms. Frontiers in gastroenterology (Lausanne, Switzerland), 5, 1864456. https://doi.org/10.3389/fgstr.2026.1864456
4. Maracle, B., Quan, S., Hamilton, P., Shaikh, A., Hazra, D., Lorenzetti, D. L., Gold, S. L., Raman, M., & St-Pierre, J. (2026). Systematic Review: Efficacy, Safety and Metabolic Outcomes of GLP-1 Receptor Agonists in Inflammatory Bowel Disease. Alimentary pharmacology & therapeutics, 63(1), 17–39. https://doi.org/10.1111/apt.70485
5. Clarke, L., Passam, R. T., Falahee, B., Jirapinyo, P., Allegretti, J. R., & Kelly, C. R. (2025). Tolerability and Effectiveness of Glucagon-Like Peptide-1 Receptor Agonists in Patients with Inflammatory Bowel Disease. Digestive diseases and sciences, 70(7), 2426–2432. https://doi.org/10.1007/s10620-025-08964-6

6. Weng, J., Alizadeh, M., & Friedman, S. (2025). Glucagon-Like Peptide-1 Receptor Agonist Therapy Does Not Increase Gastrointestinal Adverse Events in Patients with Inflammatory Bowel Disease. Digestive diseases and sciences, 70(10), 3476–3484. https://doi.org/10.1007/s10620-025-09344-w
7. Desai, A., Khataniar, H., Tabaku, F., Hashash, J. G., Farraye, F. A., & Kochhar, G. S. (2026). Efficacy of tirzepatide for weight loss and it's comparative effectiveness to weight loss surgery in inflammatory bowel disease. Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology, 45(3), 564–575. https://doi.org/10.1007/s12664-025-01835-y
8. Colwill, M., Povlsen, S., Pollok, R., Patel, K., Goodhand, J., Ahmad, T., & Honap, S. (2025). Glucagon-like peptide-1 (GLP-1) receptor agonists in inflammatory bowel disease: mechanisms, clinical implications, and therapeutic potential. Journal of Crohn's & colitis, 19(9), jjaf167. https://doi.org/10.1093/ecco-jcc/jjaf167
9. Levine, J., Lee, Y. A., Pham, A., Guo, J., Dai, H., Radwan, R. M., Bian, J., Novikov, A., & Sheer, A. (2025). Effect of Injectable Dual and Single Agonist Glucagon-Like Peptide-1 Based Therapy on Inflammatory Bowel Disease Activity Among Patients with Obesity. medRxiv : the preprint server for health sciences, 2025.11.13.25340005. https://doi.org/10.1101/2025.11.13.25340005
10. Anderson, S. R., Ayoub, M., Coats, S., McHenry, S., Tan, T., & Deepak, P. (2025). Safety and Effectiveness of Glucagon-like Peptide-1 Receptor Agonists in Inflammatory Bowel Disease. The American journal of gastroenterology, 120(5), 1152–1155. https://doi.org/10.14309/ajg.0000000000003208
11. St-Pierre, J., Klein, J., Choi, N. K., Fear, E., Pannain, S., & Rubin, D. T. (2024). Efficacy and Safety of GLP-1 Agonists on Metabolic Parameters in Non-diabetic Patients with Inflammatory Bowel Disease. Digestive diseases and sciences, 69(12), 4437–4445. https://doi.org/10.1007/s10620-024-08720-2
12. Alharbi S. H. (2024). Anti-inflammatory role of glucagon-like peptide 1 receptor agonists and its clinical implications. Therapeutic advances in endocrinology and metabolism, 15, 20420188231222367. https://doi.org/10.1177/20420188231222367
13. Wang, W., Zhang, C., Zhang, H., Li, L., Fan, T., & Jin, Z. (2023). The alleviating effect and mechanism of GLP-1 on ulcerative colitis. Aging, 15(16), 8044–8060. https://doi.org/10.18632/aging.204953
14. Hunt, J. E., Holst, J. J., Jeppesen, P. B., & Kissow, H. (2021). GLP-1 and Intestinal Diseases. Biomedicines, 9(4), 383. https://doi.org/10.3390/biomedicines9040383

15. Saadoun, A. A., Abdelsattar, A. H., Elsaid, A. H., Abdelaleam, E. A., Abdelkader, H. K., Ibrahim, H. M., Saad, M. S., Ellawi, M. S., Elsaid, R. E., Maghrabia, A., Ibrahim, D., & Ramadan, N. M. (2025). Repurposing liraglutide to the management of DSS-induced colitis: a potential for promoting autophagy. Naunyn-Schmiedeberg's archives of pharmacology, 398(12), 17173–17185. https://doi.org/10.1007/s00210-025-04339-w
16. Klein, J. A., St-Pierre, J., Choi, D., Lopez, J., & Rubin, D. T. (2024). Dramatic Changes in Thiopurine Metabolite Levels in a Patient With Inflammatory Bowel Disease Treated With Tirzepatide for Weight Loss. ACG case reports journal, 11(11), e01544. https://doi.org/10.14309/crj.0000000000001544
17. Shneyderman, M., Freid, H., Kohler, D., Peraza, J., Haskey, N., Abbott, E., Kornbluth, A., Raman, M., & Gold, S. (2024). Management of Overweight and Obesity in Patients With Inflammatory Bowel Disease. Gastroenterology & hepatology, 20(12), 712–722.
18. Villumsen, M., Schelde, A. B., Jimenez-Solem, E., Jess, T., & Allin, K. H. (2021). GLP-1 based therapies and disease course of inflammatory bowel disease. EClinicalMedicine, 37, 100979. https://doi.org/10.1016/j.eclinm.2021.100979
19. Alqinai, B., Adeniran, O., Adekolu, A., & Gayam, S. (2026). Semaglutide-Induced Symptomatic Remission in Ulcerative Colitis. ACG case reports journal, 13(4), e02070. https://doi.org/10.14309/crj.0000000000002070
20. Drucker D. J. (2026). The expanding landscape of GLP-1 medicines. Nature medicine, 32(1), 47–57. https://doi.org/10.1038/s41591-025-04124-5