

Safety profile and potential favorable reporting signals of liraglutide in patients with ulcerative colitis: A FAERS pharmacovigilance and network pharmacology study

Keliang Liu^{1#}, Xiaocui Chen^{2#}, Chunyan Li³ and Yichuan Zhang^{1*}

¹Minimally Invasive Endoscopy Center, Affiliated Hospital of Panzhihua University, Panzhihua 617000, China

²Department of Gastroenterology, The First People's Hospital of Yunnan Province, Kunming 650032, China

³Department of Gastroenterology, Affiliated Hospital of Panzhihua University, Panzhihua 617000, China

Abstract: Background: Liraglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), has preclinical anti-inflammatory and barrier-protective effects, but its safety profile and potential favorable reporting associations in ulcerative colitis (UC) remain uncertain. **Objectives:** To characterize liraglutide-associated reports in patients with UC and explore biological pathways that may contextualize the observed pharmacovigilance signals. **Methods:** Reports submitted to the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS) from January 1, 2013, to December 31, 2025, were analyzed in which liraglutide was recorded as the primary suspected drug and UC as the indication. Disproportionality was assessed using the reporting odds ratio (ROR), proportional reporting ratio (PRR), Bayesian confidence propagation neural network (BCPNN) and multi-item gamma Poisson shrinker (MGPS). Network pharmacology identified shared targets, constructed a protein-protein interaction network and performed Gene Ontology and Kyoto Encyclopedia of Genes and Genomes enrichment analyses. **Results:** Among 5,903 unique cases and 28,607 preferred-term event entries, the most frequent categories were general disorders and administration-site conditions, gastrointestinal disorders, injury or medication-related complications, infections and investigations. The term “condition aggravated” was reported in 1,512 cases. Medication management, metabolic, infectious, neuropsychiatric and gastrointestinal signals were also detected. Herpes zoster was reported in 154 cases and pneumonia-related reports included eight fatal outcomes, although concomitant immunosuppressive therapy substantially limited attribution. The reporter-coded term “pre-existing condition improved” occurred in 38 cases (ROR 25.63; 95% confidence interval 16.48-39.85) and was interpreted only as an exploratory favorable reporting association. Network pharmacology identified 84 shared candidate targets and prioritized 10 hub genes. Enriched pathways included phosphoinositide 3-kinase/protein kinase B, tumor necrosis factor and Janus kinase/signal transducer and activator of transcription signaling. **Conclusion:** FAERS findings generated safety and favorable-reporting hypotheses but did not establish incidence, causality, or therapeutic efficacy. The predicted pathways provide biological context only and require confirmation in comparator-based longitudinal studies, prospective clinical investigations and targeted experimental models.

Keywords: Drug repurposing; FAERS database; Liraglutide; Network pharmacology; Ulcerative colitis

Submitted on 26-05-2026 – Revised on 15-08-2026 – Accepted on 20-08-2026

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterized by relapsing inflammation of the colonic mucosa and an increasing global healthcare burden (Zhou *et al.*, 2026; Danese *et al.*, 2024). Current treatment commonly progresses from aminosalicylates and corticosteroids to immunomodulators, biologics and targeted small molecules, including Janus kinase (JAK) inhibitors such as tofacitinib. Despite these options, primary nonresponse, secondary loss of response, treatment burden and infection risk remain important clinical limitations (Vootukuru and Vasudevan, 2024; Chanchlani *et al.*, 2024). Additional or adjunctive approaches that modulate inflammation and support mucosal barrier function without adding substantial

systemic immunosuppression therefore warrant investigation.

Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist (GLP-1 RA) established for the treatment of type 2 diabetes and obesity (Migliorisi *et al.*, 2025). GLP-1 receptors are also expressed in the gastrointestinal tract and in immune-cell populations relevant to intestinal homeostasis (Colwill *et al.*, 2025). Experimental evidence suggests that GLP-1 receptor activation may reduce pro-inflammatory mediators, including tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β) and interleukin-6 (IL-6); support epithelial survival and repair; regulate tight-junction and barrier-protective pathways; and influence the intestinal microbiota (Wang *et al.*, 2023; Colwill *et al.*, 2025). These interconnected anti-inflammatory and barrier-protective effects provide a biological rationale for exploring liraglutide in UC, while its clinical benefit remains unconfirmed.

*Corresponding author: yashiozyc@163.com

#These authors contributed equally and are the co-first authors.

Among the clinically available GLP-1 receptor agonists, liraglutide was selected for a drug-specific and hypothesis-generating evaluation rather than because it has been demonstrated to be superior to other agents in ulcerative colitis. Liraglutide is an acylated human GLP-1 analogue with 97% sequence homology to endogenous GLP-1. Its C16 fatty-acid modification promotes reversible albumin binding and resistance to enzymatic degradation, resulting in a plasma half-life of approximately 13 hours and stable once-daily exposure (Knudsen, 2019). Importantly, liraglutide has compound-specific preclinical evidence relevant to UC pathophysiology. In a T-cell-driven adoptive transfer colitis model, liraglutide improved disease activity and attenuated colonic expression of inflammatory cytokines and chemokines, while GLP-1 signaling was associated with barrier-protective gene expression in the gastrointestinal tract (Bang-Berthelsen *et al.*, 2016). In dextran sulfate sodium (DSS)-induced colitis, liraglutide enhanced the microbiota-dependent response of interleukin-22 (IL-22)-producing group 3 innate lymphoid cells (ILC3s), a pathway implicated in epithelial repair and barrier maintenance (Sun *et al.*, 2024). More recently, liraglutide improved disease activity, colonic shortening, histopathological injury and Paneth-cell metaplasia in DSS-induced colitis, potentially through enhanced colonic autophagic flux (Saadoun *et al.*, 2025). Liraglutide has also been reported to reduce gut permeability in an experimental rat model of lipopolysaccharide-induced intestinal injury (Nozu *et al.*, 2018). Together with its relatively mature post-marketing history and the availability of a substantial number of UC-associated reports in the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS), these data supported its selection for the present drug-specific pharmacovigilance analysis. Nevertheless, no head-to-head clinical evidence has established that liraglutide is superior to other GLP-1 receptor agonists for UC; therefore, the present study should not be interpreted as a comparative or class-wide efficacy assessment.

Liraglutide is therefore a biologically plausible candidate for exploratory UC-specific pharmacovigilance analysis; however, it is not an established therapy for UC and its potential benefit remains hypothesis-generating. Nevertheless, there remains a lack of large-scale, real-world safety and effectiveness assessments for this population. Although randomized controlled trials (RCTs) can provide important safety data, they are often limited by strict inclusion criteria, small sample sizes and short follow-up periods (Lv *et al.*, 2025). Therefore, RCTs often exclude patients with complex diseases, which may not reflect the real-world clinical situation, making it difficult to capture rare adverse reactions or identify complex drug interactions (Yukselen *et al.*, 2024). To address this shortcoming, FAERS plays a key role in post-market monitoring (Lv *et al.*, 2025). FAERS contains spontaneous reports of adverse events (AEs) and supports the detection

of potential safety signals (Lv *et al.*, 2025; Jia *et al.*, 2025; Luo *et al.*, 2025b). In addition, exploratory analyses of reporter-coded favorable event terms in FAERS may generate hypotheses for potential drug repurposing; however, such findings do not constitute evidence of therapeutic efficacy. This provides a unique advantage for a comprehensive assessment of the clinical impact of drugs in the real world (Huoshen *et al.*, 2026).

FAERS is useful for detecting disproportionate reporting patterns but cannot establish the molecular basis of a drug-event association. Network pharmacology can complement pharmacovigilance by mapping predicted drug targets to disease networks and identifying candidate biological processes for experimental follow-up (Cheng *et al.*, 2025; Luo *et al.*, 2025a). A clinical-to-mechanistic triangulation strategy was therefore adopted: safety and reporter-coded favorable associations were characterized using FAERS and exploratory biological context was provided through network pharmacology. This approach does not convert a reporting signal into evidence of efficacy or mechanism.

Accordingly, this study aimed to characterize adverse-event reporting associations and reporter-coded favorable associations in FAERS reports in which liraglutide was the primary suspected drug and UC was the indication; examine clinically important co-medication patterns; and use network pharmacology to explore candidate targets and pathways that may contextualize the observed reporting patterns. All analyses were designed to generate pharmacovigilance and mechanistic hypotheses rather than to demonstrate therapeutic efficacy or causality.

MATERIALS AND METHODS

Data sources

This study integrated FAERS pharmacovigilance data with public network-pharmacology resources. FAERS reports submitted from January 1st, 2013, through December 31st, 2025, were retrieved using a targeted case-level strategy. Drug and indication records were linked within each report and cases were retained when liraglutide was coded as the primary suspected drug and ulcerative colitis was recorded as the indication. Reports were analyzed irrespective of whether type 2 diabetes, obesity, or metabolic syndrome was also reported because comorbidity information in FAERS is incomplete and non-standardized. Adverse events were standardized using the Medical Dictionary for Regulatory Activities (MedDRA, version 29.0) and summarized by preferred term (PT) and system organ class (SOC). For network pharmacology, the liraglutide structure was obtained from PubChem; candidate drug targets were predicted using the Similarity Ensemble Approach (SEA) and PharmMapper; UC-associated targets were retrieved from GeneCards, Online Mendelian Inheritance in Man

(OMIM) and the Therapeutic Target Database (TTD); and protein interactions were obtained from the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING). The overall study workflow is presented in Fig. S1.

Pharmacovigilance signal detection

Disproportionality analysis was performed within a pharmacovigilance framework to assess reporting associations between liraglutide and adverse events or favorable disease-related terms. A 2×2 contingency table was used to compare the reporting frequency of each event for liraglutide with that for all other drugs in FAERS (Table S1). Four established disproportionality approaches were applied, including the reporting odds ratio (ROR), proportional reporting ratio (PRR), Bayesian confidence propagation neural network (BCPNN) and multi-item gamma Poisson shrinker (MGPS). For ROR, a signal was defined as at least three reports with the lower bound of the two-sided 95% confidence interval (CI) exceeding 1. For PRR, a signal required at least 3 reports, $PRR \geq 2$ and $\chi^2 \geq 4$. For BCPNN, a signal was defined as a lower 2.5th percentile of the information component (IC), denoted IC025, greater than 0. For MGPS, a signal was defined as a lower 5th percentile of the empirical Bayes geometric mean (EBGM), denoted EB05, greater than 2. IC025 and EB05 are posterior lower-bound measures conventionally used in Bayesian disproportionality analysis (Table S2). A reporting signal was retained only if the prespecified threshold was met for all four algorithms. Agreement across these correlated methods was not interpreted as independent validation or evidence of causality. The unit of analysis for disproportionality testing was the individual FAERS case report. For each drug-PT pair, each unique case was counted once after removal of duplicate records for the same PT within the same case. A single case could contribute to multiple PT-specific analyses when multiple distinct events were reported. In contrast, SOC- and PT-level event counts were used for descriptive analyses and therefore may exceed the total number of unique cases. In addition to conventional safety-signal detection, an exploratory assessment of reporter-coded favorable disease-related PTs was performed. This analysis was motivated by pharmacovigilance-based drug repurposing (Böhm *et al.*, 2021), although disproportionate reporting of a favorable PT differs from the inverse adverse-event signals examined in that study (Böhm *et al.*, 2021). However, this approach was not designed to estimate clinical efficacy. In the present study, a favorable term, such as “pre-existing condition improved,” denotes the reporter’s coded observation within an individual case safety report rather than a validated clinical endpoint. Accordingly, disproportionality measures quantify disproportionate reporting within FAERS and do not estimate remission rates, mucosal healing, comparative effectiveness, incidence, or causal treatment effects (Wisniewski *et al.*, 2016; Cutroneo *et al.*, 2024; Fusaroli *et al.*, 2026). Therefore, all favorable reporting signals were

interpreted as exploratory and hypothesis-generating only. The preferred term “pre-existing condition improved” was analyzed as a reporter-coded favorable disease-related term for exploratory hypothesis generation, rather than as a validated surrogate of therapeutic efficacy. Inverse pharmacovigilance approaches may help identify repurposing hypotheses from spontaneous-reporting databases; however, disproportionality estimates do not establish clinical benefit, causality, remission, or mucosal healing (Böhm *et al.*, 2021; Cutroneo *et al.*, 2024). Data extraction, processing and signal calculations were performed using R software (version 4.3.0; R Foundation for Statistical Computing, Vienna, Austria).

Acquisition of the liraglutide structure and prediction of associated targets

The simplified molecular-input line-entry system (SMILES) string and two-dimensional molecular structure of liraglutide were obtained from PubChem. The SMILES string was submitted to the SEA database and the two-dimensional structure was submitted to PharmMapper to predict potential biological targets. Predicted targets from both sources were standardized, integrated and deduplicated to generate the liraglutide-associated target set.

Identification of disease-associated targets for UC

Disease-associated targets for ulcerative colitis (UC) were retrieved from three databases, including GeneCards, Online Mendelian Inheritance in Man (OMIM) and the Therapeutic Target Database (TTD), using “ulcerative colitis” and “UC” as search terms. To increase selection stringency, only GeneCards targets with a disease relevance score greater than 5 were retained. Subsequently, the overlapping targets shared by drugs and diseases were identified using Venny 2.1.0 (Oliveros, 2015).

GeneCards assigns a disease relevance score by integrating and weighting evidence from multiple gene-disease association resources. Because no universally accepted cutoff exists for GeneCards relevance scores across different diseases, a pragmatic stringency threshold of >5 was applied to reduce low-ranked, weakly supported associations while retaining a sufficiently broad UC-related target set for exploratory analysis. The potential influence of this empirical threshold on target selection was acknowledged as a limitation (Safran *et al.*, 2021).

Protein-protein interaction network construction and core target screening

The shared candidate targets were submitted to STRING to construct a protein-protein interaction (PPI) network. The organism was restricted to *Homo sapiens* and the minimum interaction score was set to 0.4. PPI construction was used to examine predicted functional connectivity, identify highly connected candidate nodes and distinguish network-level hypotheses for further study; it was not used to demonstrate direct liraglutide binding or validated target engagement.

Table 1: Clinical characteristics of liraglutide-associated reports in the UC subgroup from the FAERS database.

Characteristics	Case number, n	Case proportion, %
Sex		
Female	2756	46.7%
Male	2882	48.8%
Missing	265	4.5%
Weight		
< 50 kg	59	1.0%
> 100 kg	129	2.2%
50~100 kg	890	15.1%
Missing	4825	81.7%
Age		
< 18 years	71	1.2%
18 - 64.9 years	4252	72.0%
65 - 85 years	966	16.4%
> 85 years	25	0.4%
Missing	589	10.0%
Outcome		
Congenital Anomaly	3	0.1%
Death	128	2.2%
Disability	21	0.4%
Hospitalization	822	13.9%
Life-Threatening	76	1.3%
Other	4853	82.2%
Reporting year		
2013	1	0.0%
2014	9	0.2%
2015	11	0.2%
2016	9	0.2%
2017	15	0.3%
2018	118	2.0%
2019	582	9.9%
2020	967	16.4%
2021	875	14.8%
2022	1249	21.2%
2023	939	15.9%
2024	627	10.6%
2025	501	8.5%
Reporting country		
United States	4061	68.8%
Canada	1081	18.3%
Japan	226	3.8%
United Kingdom	106	1.8%
Germany	59	1.0%
Other countries	370	6.3%

The network was visualized in Cytoscape (version 3.9.1) and CytoNCA was used to calculate degree, betweenness and closeness centrality. Nodes that exceeded the median across all three measures were prioritized as candidate hubs.

Gene Ontology and Kyoto Encyclopedia of Genes and Genomes enrichment analyses

Gene Ontology (GO) functional enrichment and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment were performed in R (version 4.3.0) using clusterProfiler, enrichplot, ggplot2 and org.Hs.eg.db. GO

results were evaluated across biological process, cellular component and molecular function categories. Multiple-testing correction used the false discovery rate (FDR) and an adjusted p value <0.05 was considered statistically significant. Enrichment results were interpreted as exploratory associations derived from predicted targets rather than as experimentally confirmed mechanisms of liraglutide.

Statistical analysis

FAERS characteristics were summarized descriptively. Continuous variables were reported as medians with

interquartile ranges and categorical variables were reported as frequencies and percentages. Missing demographic values were not imputed; they were retained as a separate category and percentages were calculated using all included reports as the denominator. Cases with missing demographic information were retained in the disproportionality analyses because they were based on drug-event reporting counts rather than on covariate-adjusted models. No weight-stratified inference was performed because body weight was missing in 81.7% of reports. GO and KEGG results were corrected for multiple testing using the FDR, with adjusted p-values <0.05 considered significant. Analyses and visualizations were performed using R (version 4.3.0) and GraphPad Prism (version 10.6.0).

RESULTS

Descriptive analysis

From 2013 through 2025, 5,903 unique FAERS case reports met the inclusion criteria: liraglutide was recorded as the primary suspected drug and UC as the indication. Signal detection used ROR, PRR, BCPNN and MGPS at the individual case level for each drug-PT pair. Table 1 and Figs. 1A-1E summarize reporting country, age, sex, outcomes and annual reporting trends.

Most reports originated from the United States (68.8%), followed by Canada (18.3%), Japan (3.8%) and the United Kingdom (1.8%). Adults aged 18-64.9 years accounted for 72.0% (n=4,252) and patients aged 65 years or older accounted for 16.8% (n=991). There were 2,882 male reports (48.8%) and 2,756 female reports (46.7%). Body weight was missing in 81.7% of cases. “Other serious” outcomes accounted for 82.2%, while hospitalization, death and life-threatening outcomes were reported in 13.9% (n=822), 2.2% (n=128) and 1.3% (n=76), respectively. Reporting peaked in 2022 (n=1,249; 21.2%; Fig 1E). The reported time-to-onset distributions are presented in figure 2A; these are descriptive reporting distributions rather than estimates of population-level cumulative incidence. Concomitant UC therapies included tofacitinib, prednisone (12.3%, n=727) and mesalazine (6.6%, n=388), underscoring the potential for co-medication confounding.

AE signals at the SOC level

The 5,903 unique cases contained 28,607 PT-level event entries, as a single case could include multiple distinct events. These entries mapped to 27 SOC categories. The five most frequently reported categories were general disorders and administration-site conditions (23.00%, n=6,580), gastrointestinal disorders (20.05%, n=5,737), injury, poisoning and procedural complications (10.96%, n=3,135), infections and infestations (7.44%, n=2,129) and investigations (6.51%, n=1,861) (Table 2; Fig. 2B).

Less frequently reported categories included cardiac disorders (0.85%, n=242), blood and lymphatic system disorders (0.77%, n=219) and immune system disorders (0.72%, n=205). Endocrine disorders, pregnancy/puerperium/perinatal conditions and congenital/familial/genetic disorders each accounted for 0.07% or less of PT-level entries. These descriptive proportions do not indicate incidence or causality and the infection category is particularly susceptible to confounding by corticosteroids, JAK inhibitors, biologics, underlying UC activity and treatment selection.

AE signals at the PT level

At the PT level, 30 terms met all four prespecified disproportionality criteria (Table 3). These terms represented several clinically distinct groups: disease status terms, medication management and administration errors, metabolic laboratory abnormalities, infectious events, neuropsychiatric symptoms, gastrointestinal symptoms and one reporter-coded favorable disease-related term. At the PT level, “condition aggravated” was the most frequently reported term (n=1,512) and met all four prespecified criteria (ROR 3.56; 95% CI 3.37-3.76; PRR 3.43; EBGM 3.16; JC 1.66). Twelve reports coded with this term had a fatal outcome. Because UC has a relapsing-remitting course and FAERS lacks standardized baseline disease activity and treatment timing information, this association cannot be interpreted as evidence that liraglutide caused worsening of disease.

Medication-management terms were reported with high frequency and disproportionately. “Product dose omission in error” occurred in 319 cases (ROR 178.16; 95% CI 132.20-240.10) and “intentional product misuse” occurred in 207 cases (ROR 22.40; 95% CI 18.64-26.91). Additional terms included product dose omission, intentional dose omission, prescribed overdose, prescribing error and dispensing error. These reports may reflect administration problems, adherence barriers, polypharmacy, or treatment complexity rather than direct pharmacological toxicity.

Metabolic, infectious, neuropsychiatric and gastrointestinal terms were also identified. Increased blood cholesterol was reported in 245 cases (ROR 10.59; 95% CI 9.14-12.27) and increased blood triglycerides were reported in 29 cases (ROR 12.15; 95% CI 7.85-18.80). Herpes zoster was reported in 154 cases (ROR 3.14; 95% CI 2.66-3.71) and pneumonia-related reports included eight fatal outcomes. Sleep disorder (n=163), memory impairment (n=158) and depressed mood (n=113) were the main neuropsychiatric terms. Gastrointestinal terms included bowel movement irregularity (n=113) and the MedDRA PT “abnormal faeces” (n=65). These symptoms overlap with UC manifestations, recognized gastrointestinal effects of GLP-1 RA and concomitant therapies; therefore, drug-specific attribution is not possible.

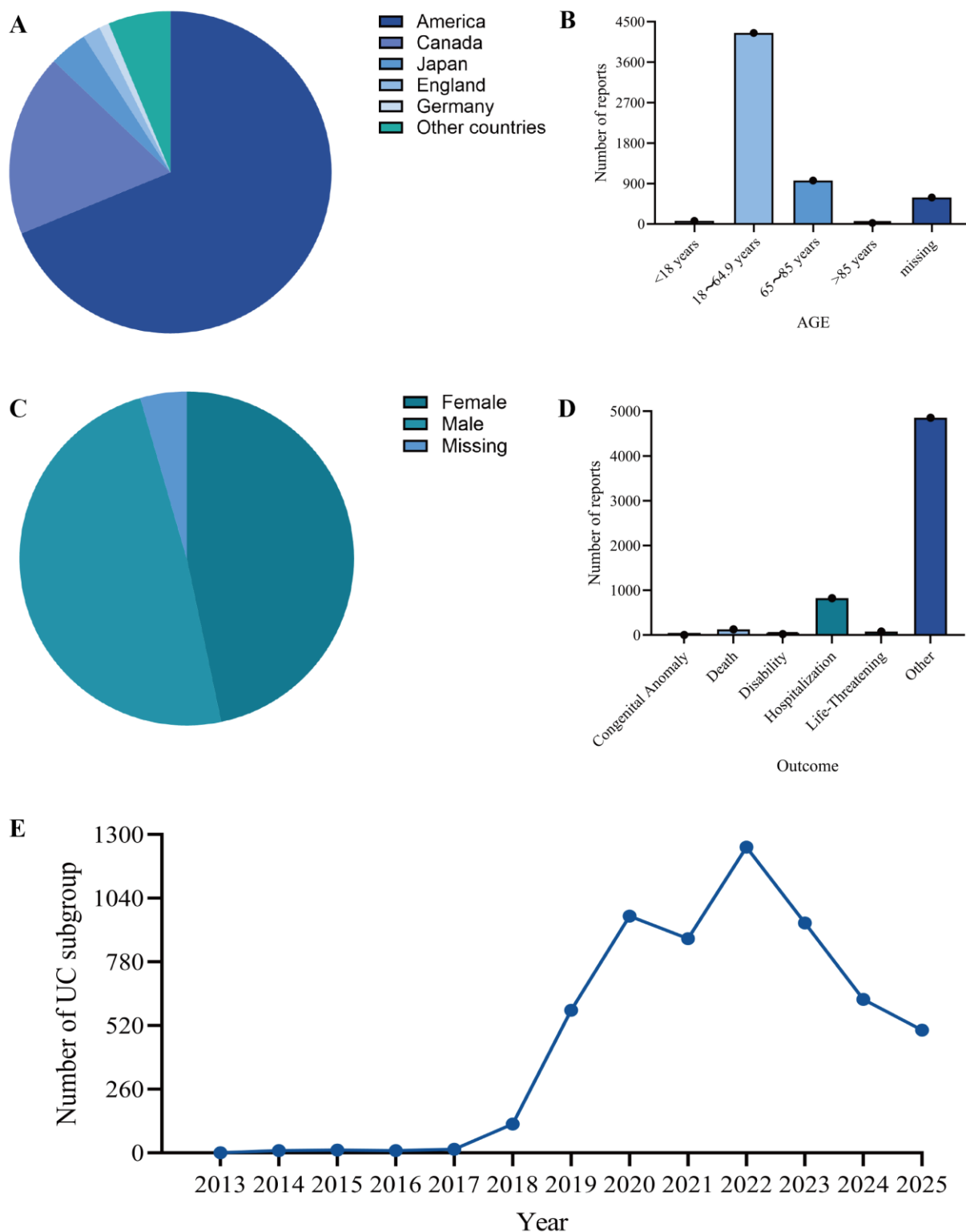


Fig. 1: Clinical characteristics and temporal trends of liraglutide-associated reports in the UC subgroup from the FAERS database. (A) Reporting country; (B) Age distribution; (C) Sex distribution; (D) Reported outcomes; (E) Annual numbers of included case reports from 2013 to 2025. Percentages in panels A and C were calculated using all 5,903 included reports as the denominator. Panels B, D and E show the number of reports.

Table 2: Distribution of AE signals (SOC) of liraglutide in various system organ categories.

S. No, n	SOC	Case number, n	Case proportion, %
1	General disorders and administration site conditions	6580	23.00%
2	Gastrointestinal disorders	5737	20.05%
3	Injury, poisoning and procedural complications	3135	10.96%
4	Infections and infestations	2129	7.44%
5	Investigations	1861	6.51%
6	Nervous system disorders	1556	5.44%
7	Musculoskeletal and connective tissue disorders	1248	4.36%
8	Psychiatric disorders	1143	4.00%
9	Skin and subcutaneous tissue disorders	1063	3.72%
10	Respiratory, thoracic and mediastinal disorders	925	3.23%
11	Vascular disorders	560	1.96%
12	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	367	1.28%
13	Surgical and medical procedures	313	1.09%
14	Metabolism and nutrition disorders	274	0.96%
15	Renal and urinary disorders	270	0.94%
16	Eye disorders	252	0.88%
17	Cardiac disorders	242	0.85%
18	Blood and lymphatic system disorders	219	0.77%
19	Immune system disorders	205	0.72%
20	Social circumstances	153	0.53%
21	Hepatobiliary disorders	114	0.40%
22	Ear and labyrinth disorders	114	0.40%
23	Reproductive system and breast disorders	85	0.30%
24	Endocrine disorders	20	0.07%
25	Pregnancy, puerperium and perinatal conditions	20	0.07%
26	Congenital, familial and genetic disorders	15	0.05%
27	Product issues	7	0.02%

The reporter-coded PT “pre-existing condition improved” was reported in 38 cases and met the disproportionality criteria (ROR 25.63; 95% CI 16.48-39.85; PRR 25.60; EBGM 13.76; IC 3.78). This is an exploratory favorable reporting association, not a validated efficacy endpoint. FAERS does not contain standardized disease-activity scores, endoscopic outcomes, mucosal-healing assessments, steroid-free remission, or longitudinal treatment response. The term may reflect subjective reporting, spontaneous fluctuation, concomitant UC treatment, nonspecific improvement, or reporting practice.

Identification of intersecting targets and PPI network analysis

After integration and deduplication, 280 predicted liraglutide-associated targets and 1,118 UC-associated targets were identified. Their intersection contained 84 shared candidate targets. The overlap count is reported in the text and the original Venn diagram was removed because it did not add essential information. These shared targets were carried forward for PPI and enrichment analyses; they should not be interpreted as confirmed therapeutic targets or direct drug-disease interactions. The STRING-derived PPI network contained 84 candidate nodes and their predicted functional associations (Fig. 3A). CytoNCA analysis prioritized 10 highly connected

candidate hubs: TNF (tumor necrosis factor), IL6 (interleukin-6), IL1B (interleukin-1 beta), ALB (albumin), AKT1 (AKT serine/threonine kinase 1), INS (insulin), TP53 (tumor protein p53), MMP9 (matrix metalloproteinase 9), TLR4 (Toll-like receptor 4) and STAT3 (signal transducer and activator of transcription 3) (Fig. 3B). Gene symbols are used for network nodes, whereas protein names are used when discussing biological functions. These genes are established regulators of inflammation, metabolism and barrier biology. Their network centrality supports prioritization for further study but does not demonstrate direct liraglutide binding, UC specificity, or a validated therapeutic mechanism.

GO functional and KEGG pathway enrichment analyses

GO functional enrichment and KEGG pathway enrichment were performed for the 84 shared candidate targets. GO enrichment was observed in the biological process, cellular component and molecular function categories (Figs. 4A and 4B). Prominent biological-process terms included inflammatory-response regulation, responses to lipopolysaccharide and regulation of interleukin signaling. Cellular-component terms included vesicle lumen and membrane microdomains, whereas molecular-function terms included cytokine-receptor binding, G-protein-coupled receptor binding and protein-kinase regulatory

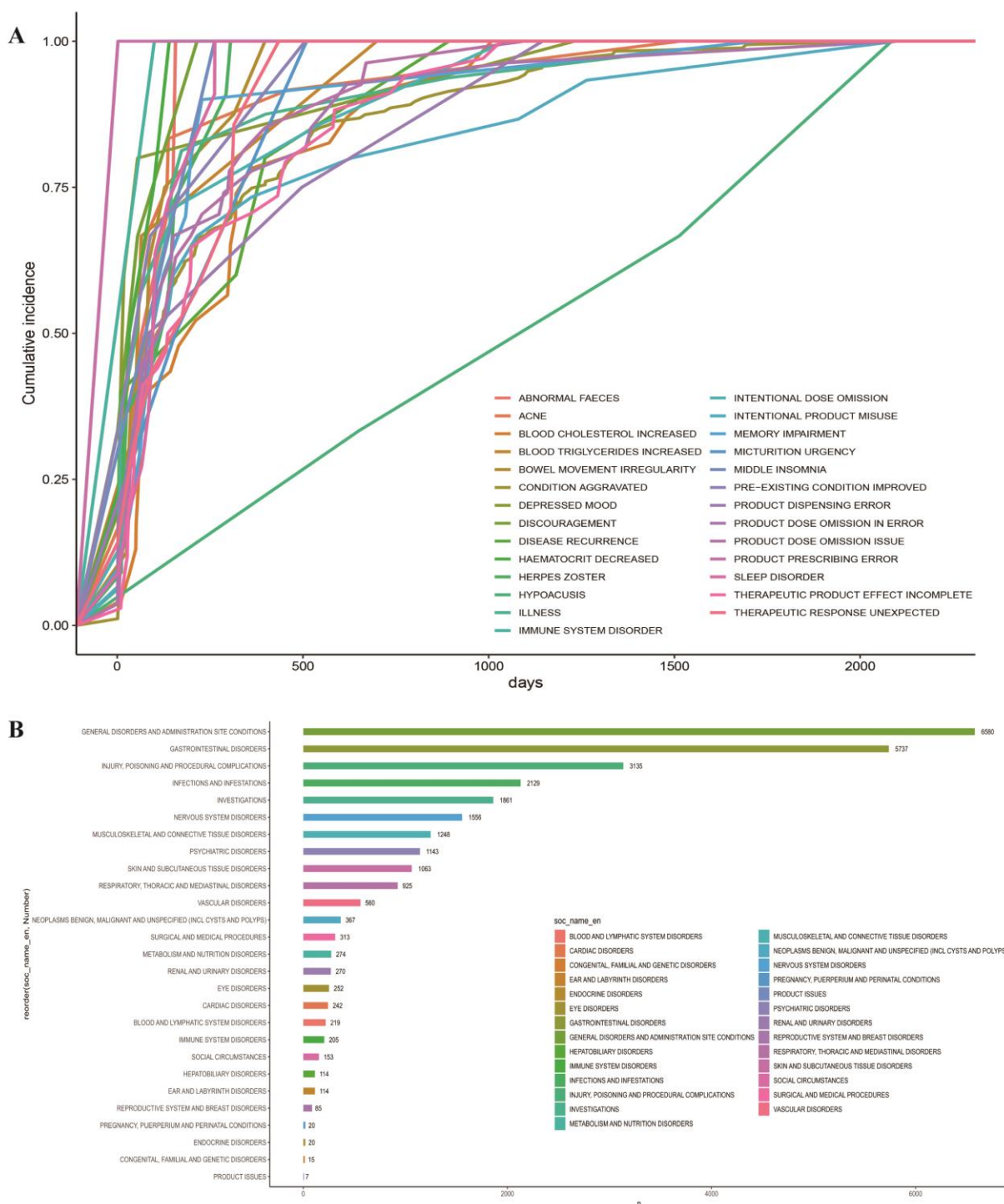


Fig. 2: Time-to-onset and distribution of adverse events associated with liraglutide. (A) Time of occurrence of adverse events; (B) Number of SOC occurrences. Percentages in panel B are calculated using the 28,607 PT-level event entries as the denominator.

activity. These results describe enrichment within the predicted target set and require experimental validation. KEGG enrichment highlighted phosphoinositide 3-kinase/protein kinase B (PI3K-Akt), TNF and JAK/signal transducer and activator of transcription (JAK-STAT) signaling (Figs. 4C and 4D). These pathways are broadly

involved in epithelial survival, cytokine signaling, immune cell activation and mucosal barrier regulation in UC and other inflammatory disorders. Their enrichment provides biological plausibility for further investigation but does not establish a liraglutide-specific mechanism or prove that liraglutide produces therapeutic benefit in UC.

Table 3: The top 30 positive signals of liraglutide in the PT level in the COLITIS Ulcerative subgroup.

S. No. , n	Pathological report, case	PT	ROR (95%CI)	PRR (χ^2)	EBGM (EB05)	IC (IC025)
1.	1512	Condition aggravated	3.56 (3.37-3.76)	3.43 (2352.95)	3.16 (2.99)	1.66 (1.58)
2.	537	Product dose omission issue	2.71 (2.48-2.97)	2.68 (520.43)	2.53 (2.32)	1.34 (1.21)
3.	450	Therapeutic product effect incomplete	4.94 (4.47-5.47)	4.88 (1183.78)	4.3 (3.88)	2.1 (1.95)
4.	319	Product dose omission in error	178.16 (132.2-240.1)	176.19 (7532.94)	24.74 (18.36)	4.63 (4.3)
5.	245	Blood cholesterol increased	10.59 (9.14-12.27)	10.51 (1528.2)	7.89 (6.8)	2.98 (2.73)
6.	218	Acne	5.35 (4.62-6.18)	5.31 (641.26)	4.62 (3.99)	2.21 (1.97)
7.	207	Intentional product misuse	22.4 (18.64-26.91)	22.24 (2327.4)	12.77 (10.63)	3.67 (3.35)
8.	173	Illness	3.08 (2.63-3.6)	3.06 (216.78)	2.86 (2.44)	1.51 (1.27)
9.	163	Sleep disorder	8.63 (7.24-10.3)	8.59 (834.53)	6.79 (5.69)	2.76 (2.46)
10.	158	Memory impairment	5.1 (4.3-6.05)	5.08 (437.79)	4.45 (3.75)	2.15 (1.87)
11.	154	Herpes zoster	3.14 (2.66-3.71)	3.13 (200.8)	2.91 (2.46)	1.54 (1.28)
12.	140	Therapeutic response unexpected	17.42 (14.09-21.52)	17.34 (1324.64)	11.04 (8.93)	3.46 (3.07)
13.	113	Depressed mood	5.5 (4.49-6.74)	5.48 (345.97)	4.74 (3.87)	2.25 (1.9)
14.	113	Bowel movement irregularity	8.4 (6.8-10.37)	8.37 (562.82)	6.65 (5.39)	2.73 (2.36)
15.	65	Abnormal faeces	2.88 (2.23 - 3.72)	2.88 (72.13)	2.7 (2.09)	1.43 (1.02)
16.	64	Intentional dose omission	6.04 (4.61-7.92)	6.03 (220.6)	5.13 (3.91)	2.36 (1.88)
17.	58	Prescribed overdose	7.98 (5.96-10.69)	7.97 (274.4)	6.41 (4.78)	2.68 (2.13)
18.	52	Product prescribing error	3.05 (2.29-4.07)	3.05 (64.52)	2.85 (2.14)	1.51 (1.04)
19.	44	Discouragement	12.54 (8.78-17.92)	12.53 (321.11)	8.93 (6.25)	3.16 (2.42)
20.	43	Hypoacusis	4.72 (3.41-6.52)	4.71 (107.46)	4.17 (3.02)	2.06 (1.49)
21.	42	Disease recurrence	3.96 (2.87-5.48)	3.96 (81.26)	3.59 (2.6)	1.84 (1.29)
22.	39	Middle insomnia	8.77 (6.11-12.57)	8.76 (203.48)	6.89 (4.8)	2.78 (2.07)
23.	38	Pre-existing condition improved	25.63 (16.48-39.85)	25.6 (466.15)	13.76(8.85)	3.78 (2.8)
24.	35	Product dispensing error	5.23 (3.64-7.51)	5.22 (100.57)	4.55 (3.17)	2.19 (1.53)
25.	32	Therapeutic product effect delayed	4.78 (3.28-6.96)	4.78 (81.49)	4.22 (2.9)	2.08 (1.4)
26.	29	Blood triglycerides increased	12.15 (7.85-18.8)	12.13 (205.86)	8.74 (5.64)	3.13 (2.18)
27.	25	Micturition urgency	4.4 (2.88 - 6.71)	4.4 (56.62)	3.93 (2.58)	1.97 (1.21)
28.	24	Haematocrit decreased	3.66 (2.39 - 5.61)	3.66 (41.01)	3.35 (2.19)	1.74 (1)
29.	24	Immune system disorder	3.64 (2.38 - 5.58)	3.64 (40.64)	3.33 (2.18)	1.74 (0.99)
30.	23	Laboratory test abnormal	3.57 (2.31 - 5.51)	3.57 (37.66)	3.27 (2.12)	1.71 (0.95)

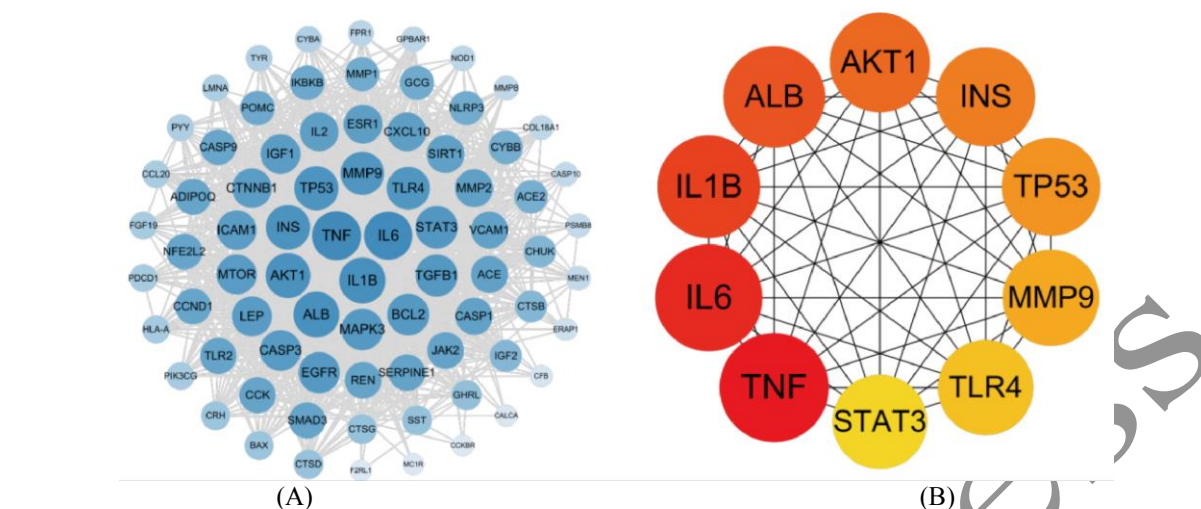


Fig. 3: Protein-protein interaction analysis of the 84 shared candidate targets. (A) STRING-derived interaction network; (B) Ten topologically prioritized candidate hub genes.

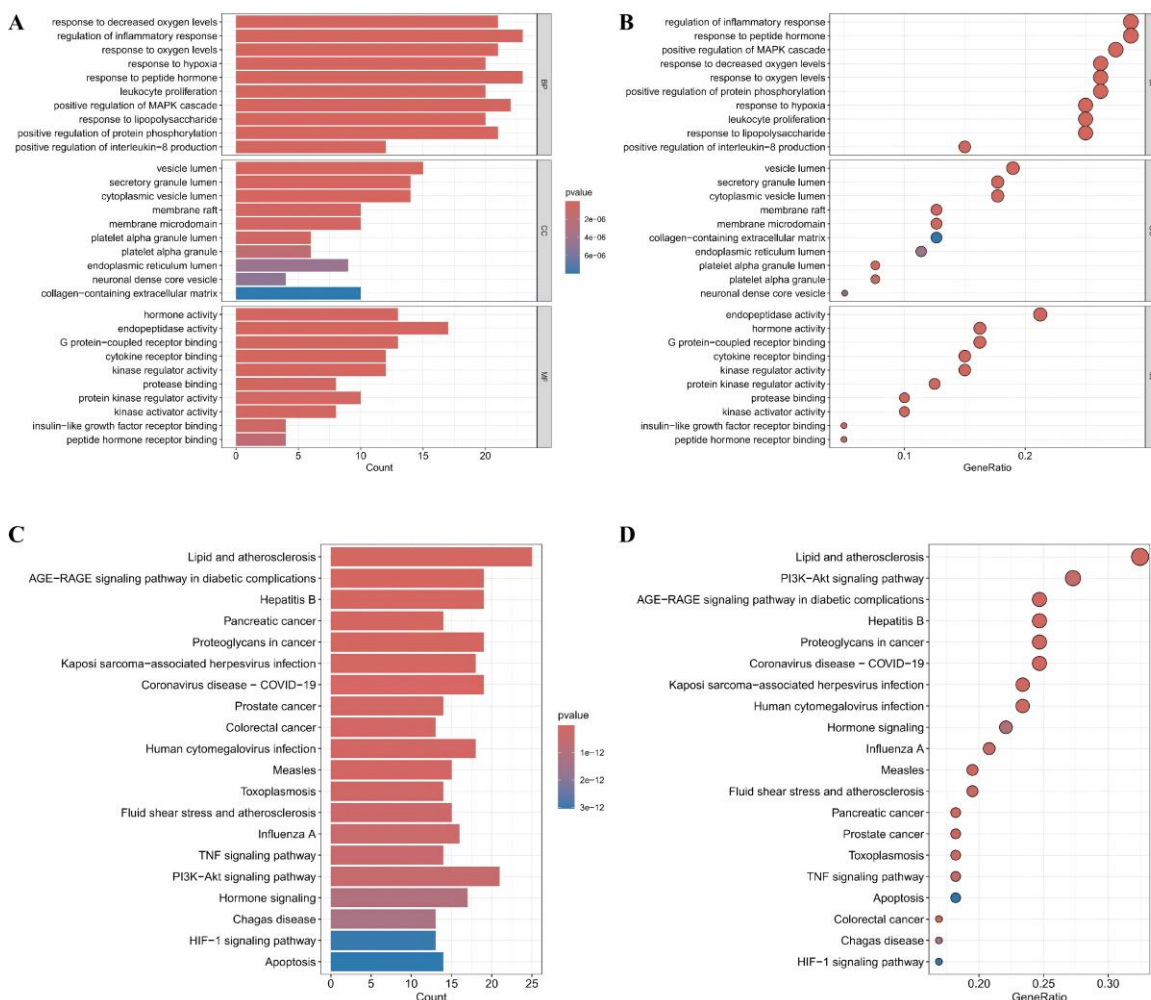


Fig. 4: GO and KEGG enrichment analysis of the intersecting targets. (A) Bar plot of the top enriched Gene Ontology (GO) terms across biological process, cellular component, and molecular function categories; (B) Bubble plot of the corresponding GO terms; (C) Bar plot of the top enriched Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways; (D) Bubble plot of the corresponding KEGG pathways.

DISCUSSION

This study combined case-level FAERS signal detection with network pharmacology to characterize liraglutide-associated reporting patterns in a UC subgroup. The principal findings were expected gastrointestinal signals, medication management problems, metabolic and neuropsychiatric terms, infection-related reports and an exploratory reporter-coded favorable association. Because FAERS lacks an exposure denominator, standardized disease activity and adequate control of concomitant treatment, none of these findings establish incidence, causality, or efficacy (Cutroneo *et al.*, 2024; Fusaroli *et al.*, 2026). The network analysis similarly provides candidate biological context rather than mechanistic confirmation.

An exploratory favorable reporting association was identified for the reporter-coded PT “pre-existing condition improved”; this finding reflects disproportionate reporting only and should not be interpreted as evidence of clinical improvement, therapeutic efficacy, or reduced UC disease activity (Böhm *et al.*, 2021; Cutroneo *et al.*, 2024). Experimental literature suggests several biologically plausible intestinal actions of GLP-1 receptor signaling. Reduced inflammatory signaling and barrier-protective responses have been reported in colitis models (Bang-Berthelsen *et al.*, 2016; Wang *et al.*, 2023). Microbiota-dependent changes in IL-22-producing ILC3s and epithelial tight-junction proteins were described by Sun *et al.* (2024), while autophagic responses and intestinal permeability were investigated in distinct liraglutide-treated experimental models (Saadoun *et al.*, 2025; Nozu *et al.*, 2018). These findings provide preclinical context and cannot establish efficacy in patients with UC. The PPI analysis prioritized TNF, IL6, IL1B and STAT3 and KEGG enrichment included PI3K-Akt, TNF and JAK-STAT signaling. These findings are compatible with recognized inflammatory and barrier-related biology. The clinical relevance of TNF is supported by randomized trials of infliximab in UC (Rutgeerts *et al.*, 2005). However, prioritization of an inflammatory hub such as IL-6 indicates network connectivity rather than a validated liraglutide target or an established indication for IL-6-directed treatment. Thus, the hub analysis indicates that the predicted network captures recognized UC biology; it does not show that liraglutide directly engages TNF, IL-6, or JAK-STAT components.

The most clinically concerning reporting pattern involved infection-related events, particularly herpes zoster and pneumonia, including eight pneumonia-associated fatal outcomes. These signals cannot be attributed specifically to liraglutide. Tofacitinib was highlighted as a major confounder because it was frequently reported as a concomitant UC therapy and is a JAK inhibitor with a well-characterized association with herpes zoster and serious infection (Winthrop *et al.*, 2021; Sandborn *et al.*, 2023;

Panes *et al.*, 2024). Concomitant immunosuppression, older age, comorbidity and active disease are relevant considerations when interpreting infection risk in IBD (Yanai *et al.*, 2026). FAERS does not reliably capture treatment timing, dose, duration, overlap, vaccination status, or disease severity; therefore, the contributions of liraglutide, concomitant treatment and underlying disease cannot be separated and the extent of co-medication confounding cannot be quantified.

Clinical monitoring and precautionary considerations

When liraglutide is prescribed for an approved metabolic indication in a patient with UC, clinical monitoring should account for both the metabolic treatment and concomitant UC therapies. Active or recent infection, vaccination status, immunosuppressive exposure and relevant comorbidity should be reviewed in accordance with infection-prevention guidance for IBD (Yanai *et al.*, 2026). Persistent vomiting or diarrhea, dehydration and worsening gastrointestinal symptoms warrant assessment; renal function should be monitored when gastrointestinal adverse reactions may cause volume depletion, consistent with liraglutide prescribing information (National Library of Medicine, 2026). Glucose and other metabolic parameters should be assessed according to the underlying indication and concomitant medications. Medication reconciliation, injection education and assessment of missed doses may help address treatment complexity and adherence barriers, which have been documented in IBD populations (Kochar *et al.*, 2024; Ramos *et al.*, 2022; Brenner *et al.*, 2023). Fever, respiratory symptoms, or a vesicular rash require prompt clinical evaluation, particularly during immunosuppressive treatment (Yanai *et al.*, 2026). These considerations derive from established clinical guidance and the limitations of the observed reports; they are not a validated study-specific monitoring protocol or a recommendation to initiate liraglutide as UC therapy. The integrated framework used here is best described as clinical-to-mechanistic triangulation. FAERS identifies clinical reporting patterns and potential confounders, while network pharmacology tests whether predicted drug-associated targets overlap with disease-relevant networks and pathways. Agreement between these layers can prioritize hypotheses but cannot cross-validate efficacy or causality (Cheng *et al.*, 2025; Fusaroli *et al.*, 2026). Before liraglutide could be considered a standard UC therapy, future work should include longitudinal active-comparator studies with validated exposure and co-medication data; stratification by diabetes, obesity, disease activity and immunosuppressive treatment; standardized clinical, biochemical, endoscopic and steroid-free remission outcomes; temporal and dose-response analyses; experimental confirmation of target engagement in intestinal epithelial and immune-cell models; validation in relevant colitis models; and ultimately adequately powered randomized clinical trials with predefined safety monitoring.

Study limitations

This study has several limitations. First, FAERS is a spontaneous reporting system without a known exposed population; therefore, incidence, absolute risk and comparative risk cannot be calculated. Reports are subject to underreporting, stimulated or selective reporting, duplicate or incomplete entries, notoriety effects and differential healthcare utilization (Cutroneo *et al.*, 2024; Fusaroli *et al.*, 2026). Second, clinical information is non-standardized and frequently missing. Body weight was unavailable in 81.7% of reports and FAERS did not provide consistent definitions for UC severity, endoscopic findings, laboratory markers, treatment indication, dose, duration, adherence, or outcome. Third, confounding by indication is likely because liraglutide is prescribed primarily for diabetes or obesity and these conditions may affect treatment selection, comorbidity, co-medication and reporting behavior. Fourth, co-medication confounding is substantial in UC, especially for infection signals associated with corticosteroids, immunomodulators, biologics and JAK inhibitors (Winthrop *et al.*, 2021; Yanai *et al.*, 2026). The available data did not support reliable exclusion-based, stratified, or adjusted analyses. Fifth, reporter-coded favorable terms are subjective and may reflect spontaneous disease fluctuation, concomitant treatment, nonspecific improvement, or coding practice; they are not efficacy endpoints. Finally, network pharmacology relies on *in-silico* databases and algorithm-based interactions that may yield false-positive, nonspecific, or topology-biased targets. The GeneCards threshold was empirical and the GO/KEGG pathways were not independently validated. Database-derived gene associations do not constitute experimental confirmation of target engagement (Safran *et al.*, 2021). These limitations require cautious, hypothesis-generating interpretation.

CONCLUSION

FAERS identified exploratory safety and favorable reporting associations in liraglutide-associated UC reports, including gastrointestinal, infection-related, metabolic, neuropsychiatric, disease status and medication management terms. The reporter-coded term “pre-existing condition improved” does not establish clinical benefit and infection-related findings remained susceptible to substantial confounding by concomitant immunosuppressive therapy. Network pharmacology identified 84 shared candidate targets and inflammatory or barrier-related pathways that provide only preliminary biological context. Prospective clinical studies, active-comparator pharmacoepidemiologic analyses and targeted experimental validation are required before liraglutide can be evaluated as a therapeutic option for UC.

Acknowledgments

None.

Authors' contributions

Keliang Liu and Xiaocui Chen: Conceptualization, design and methodology. Keliang Liu: Formal analysis and visualization; Chunyan Li and Yichuan Zhang: Validation; Xiaocui Chen: Data acquisition; Keliang Liu and Xiaocui Chen: Writing-original draft; Keliang Liu, Xiaocui Chen and Yichuan Zhang: Writing-review and editing.

Funding

There was no funding.

Data availability statement

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request. The source FAERS data are publicly accessible through the U.S. Food and Drug Administration.

Ethical approval

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

Consent to participate

All data in this study were secondhand and derived from public databases.

REFERENCES

- Anbazhagan AN, Thaqi M, Priyamvada S, Jayawardena D, Kumar A, Gujral T, Chatterjee I, Mugarza E, Saxena S, Onyuksel H and Dudeja PK (2017). GLP-1 nanomedicine alleviates gut inflammation. *Nanomedicine*, **13**(2): 659-665.
- Ansari HUH, Qazi SU, Sajid F, Altaf Z, Ghazanfar S, Naveed N, Ashfaq AS, Siddiqui AH, Iqbal H and Qazi S (2024). Efficacy and safety of glucagon-like peptide-1 receptor agonists on body weight and cardiometabolic parameters in individuals with obesity and without diabetes: A systematic review and meta-analysis. *Endocr. Pract.*, **30**(2): 160-171.
- Bang-Berthelsen CH, Holm TL, Pyke C, Simonsen L, Sokilde R, Pociot F, Heller RS, Folkersen L, Kvist PH, Jackerott M, Fleckner J, Vilien M, Knudsen LB, Heding A and Frederiksen KS (2016). GLP-1 induces barrier-protective expression in Brunner glands and regulates colonic inflammation. *Inflamm. Bowel. Dis.*, **22**(9): 2078-2097.
- Barry D, Thachuk C and Trink J (2025). Integrating gut microbiome and host transcriptomics for the personalized management of IBD. *Epigenomics*, **17**(18): 1503-1512.
- Bayoumy AB, Clarke LM, Deepak P, Desai A, Sehgal P, Gorelik U, Bar-Yoseph H, Villumsen M, Mulder CJJ, Stenvers DJ, Tushuizen ME and de Boer NKH (2025). Glucagon-like peptide 1 receptor agonists and the clinical outcomes of inflammatory bowel disease: A systematic review and meta-analysis. *J. Crohns. Colitis.*, **19**(10): jjaf181.

- Birda CL, Ibrahim F, Chatterjee A, Jena A, Sharma V and Sebastian S (2026). Impact of GLP-1 analogues on immune-mediated inflammatory diseases: A systematic review. *Autoimmun. Rev.*, **25**(1): 103936.
- Böhm R, Bulin C, Waetzig V, Cascorbi I, Klein HJ and Herdegen T (2021). Pharmacovigilance-based drug repurposing: The search for inverse signals via OpenVigil identifies putative drugs against viral respiratory infections. *Br. J. Clin. Pharmacol.*, **87**(11): 4421-4431.
- Brenner EJ, Long MD, Kappelman MD, Zhang X, Sandler RS and Barnes EL (2023). Development of an inflammatory bowel disease-specific medication adherence instrument and reasons for non-adherence. *Dig. Dis. Sci.*, **68**(1): 58-64.
- Brockmann L, Ronda C, Schwanz LT, Qu Y, Shneider DW, Mavros CF, Ivanov II, Bhagat G and Wang HH (2025). Engineered probiotic restores GLP-1 signaling to ameliorate fiber-deficiency exacerbated colitis. *Sci. Adv.*, **11**(45): eadx6869.
- Chanchlani N, Lin S, Bewshea C, Hamilton B, Thomas A, Smith R, Roberts C, Bishara M, Nice R, Lees CW, Sebastian S, Irving PM, Russell RK, McDonald TJ, Goodhand JR, Ahmad T, Kennedy NA and PANTS Consortium (2024). Mechanisms and management of loss of response to anti-TNF therapy for patients with Crohn's disease: 3-year data from the prospective, multicentre PANTS cohort study. *Lancet Gastroenterol. Hepatol.*, **9**(6):521-538.
- Chen Y, Huang L, Li W, Gu H and Chen Y (2025). Exploring skin adverse events and mechanisms of apalutamide using data mining algorithms and network pharmacology. *Front. Pharmacol.*, **16**: 1517874.
- Cheng Y, Yang Y, Su Y, Chen R, Qian D and Xu J (2025). FAERS based disproportionality analysis and network pharmacology investigation of taxanes associated drug induced liver injury. *Sci. Rep.*, **15**(1): 15137.
- Chung CS, Lee WW and Le PH (2025). Upadacitinib as rescue therapy for corticosteroid failure acute severe ulcerative colitis: An Asian experience from Taiwan. *Int. J. Colorectal. Dis.*, **40**(1): 33.
- Colombel JF (2018). Herpes Zoster in patients receiving JAK inhibitors for ulcerative colitis: Mechanism, epidemiology, management and prevention. *Inflamm. Bowel. Dis.*, **24**(10): 2173-2182.
- Colwill M, Povlsen S, Pollok R, Patel K, Goodhand J, Ahmad T and Honap S (2025). Glucagon-like peptide-1 (GLP-1) receptor agonists in inflammatory bowel disease: mechanisms, clinical implications and therapeutic potential. *J. Crohns. Colitis.*, **19**(9): jjaf167.
- Cutroneo PM, Sartori D, Tuccori M, Crisafulli S, Battini V, Carnovale C, Rafaniello C, Capuano A, Poluzzi E, Moretti U and Raschi E (2024). Conducting and interpreting disproportionality analyses derived from spontaneous reporting systems. *Front. Drug Saf. Regul.*, **3**: 1323057.
- Dal Buono A, Armuzzi A, Caprioli F, Castiglione F, Danese S, Gionchetti P, Lazzari D, Leone S, Orlando A, Vecchi M and Generazione Aderenza Study Group (2025). Therapeutic adherence in inflammatory bowel disease: User guide from a multidisciplinary modified Delphi consensus. *Dig. Liver Dis.*, **57**(7): 1403-1410.
- Danese S, Dignass A, Matsuoka K, Ferrante M, Long M, Redondo I, Moses R, Maier S, Hunter Gible T, Morris N, Milch C and Abreu MT (2024). Early and sustained symptom control with mirikizumab in patients with ulcerative colitis in the phase 3 LUCENT programme. *J. Crohns. Colitis.*, **18**(11): 1845-1856.
- Dasharathy SS, Long MD, Lackner JM, Ben-Ami Shor D, Yang L, Bar N, Ha C and Weiss GA (2023). Psychological factors associated with adherence to oral treatment in ulcerative colitis. *Inflamm. Bowel. Dis.*, **29**(1): 97-102.
- Fusaroli M, Mitchell J, Rudolph A, Rocca E and Fusaroli R (2026). Causal inference tools for pharmacovigilance: Using causal graphs to identify and address biases in disproportionality analysis. *Drug Saf.*, **49**(4): 449-469.
- Galloway J, Raine T, Rivett L, Roberts J, Dews SA and Choy EH (2022). Herpes zoster and Janus kinase inhibition in rheumatology and gastroenterology patients: Managing risk and vaccination. *Clin. Exp. Rheumatol.*, **40**(7): 1432-1441.
- Gialouri CG, Moustafa S, Thomas K, Hadziyannis E and Vassilopoulos D (2023). Herpes zoster in patients with inflammatory arthritides or ulcerative colitis treated with tofacitinib, baricitinib or upadacitinib: A systematic review of clinical trials and real-world studies. *Rheumatol. Int.*, **43**(3):421-435.
- Green KM, Shin SM, Jha RK and Kumar A (2026). Current and emerging approaches to manage chronic inflammatory gut disorders. *Front. Cell Infect. Microbiol.*, **16**:1762119.
- He Y, Wang Y, Lv J, Luo X and Xia Q (2026). Real-world safety signals of baricitinib and *in-silico* exploration of a potential mechanism underlying herpes zoster: A multidisciplinary analysis. *Naunyn. Schmiedeberg's Arch. Pharmacol.*, **399**(9): 14039-14053.
- Huoshen W, Xiong J, Ma X, Wang H, Cheng P, Chen X, Shuai G, Chen Y, Zhang X, Sun C, Li C and Shi R (2026). Pharmacovigilance-based identification and mechanistic exploration of periodontitis-related drugs. *J. Clin. Periodontol.*, **53**(1):117-126.
- Jia P, Zhou Y, Gao Y, Wang S, Yin J, Lian Y and Lai Q (2025). Real-world pharmacovigilance investigation of imipenem/cilastatin: Signal detection using the FDA adverse event reporting system (FAERS) database. *Front. Pharmacol.*, **16**: 1524159.
- Knudsen LB (2019). Inventing liraglutide, a glucagon-like peptide analogue, for the treatment of diabetes and obesity. *ACS Pharmacol. Transl. Sci.*, **2**(6): 468-484.
- Kochar B, Rusher A, Araka E, Glasser R, Lai J, Ritchie C and Ananthakrishnan AN (2024). Prevalence and appropriateness of polypharmacy in older adults with

- inflammatory bowel diseases. *Dig. Dis. Sci.*, **69**(3):766-774.
- Luo J, Chen S, Zhang M, Gao Y and Zeng Y (2025). Pharmacovigilance and signal detection of adverse drug events associated with proteasome inhibitors in multiple myeloma: A real-world analysis using the FAERS database. *Hematology*, **30**(1): 2534758.
- Luo ZY, Li X, Chen CT, Kang HH, Zhang ZJ, Wang D and Gong JR (2025). Ocular adverse events associated with GLP-1 receptor agonists: A real-world study based on the FAERS database and network pharmacology. *Expert Opin. Drug Saf.*, **24**(3): 287-296.
- Lv L, Wu X, Ren Y, Guo Y, Wang H and Li X (2025). Postmarketing safety evaluation of pemetrexed using FAERS and JADER databases. *Sci. Rep.*, **15**(1):18738.
- Mahdy RNE, Nader MA, Helal MG, Abu-Risha SE and Abdelmageed ME (2025). Protective effect of Dulaglutide, a GLP1 agonist, on acetic acid-induced ulcerative colitis in rats: Involvement of GLP-1, TFF-3 and TGF- β /PI3K/NF- κ B signaling pathway. *Naunyn Schmiedeberg's Arch. Pharmacol.*, **398**(5): 5611-5628.
- Migliorisi G, Gabbiadini R, Dal Buono A, Ferraris M, Privitera G, Petronio L, Bertoli P, Bezzio C and Armuzzi A (2025). GLP-1 receptor agonists in IBD: Exploring the crossroads of metabolism and inflammation. *Front. Immunol.*, **16**: 1610368.
- Moiz A, Filion KB, Toutounchi H, Tsoukas MA, Yu OHY, Peters TM and Eisenberg MJ (2025). Efficacy and safety of glucagon-like peptide-1 receptor agonists for weight loss among adults without diabetes: A systematic review of randomized controlled trials. *Ann. Intern. Med.*, **178**(2): 199-217.
- National Library of Medicine (2026). DailyMed: Liraglutide injection, prescribing information. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=14bf9812-14ee-46ce-93b1-686e4906cbbc> (Accessed 8 September 2026).
- Nozu T, Miyagishi S, Kumei S, Nozu R, Takakusaki K and Okumura T (2018). Glucagon-like peptide-1 analog, liraglutide, improves visceral sensation and gut permeability in rats. *J. Gastroenterol. Hepatol.*, **33**(1): 232-239.
- Oliveros JC (2015). Venny. An interactive tool for comparing lists with Venn's diagrams (2007-2015), version 2.1.0. Available at: <https://bioinfogp.cnb.csic.es/tools/venny/index.html> (Accessed 8 September 2026).
- Panés J, D'Haens GR, Sands BE, Ng SC, Lawendy N, Kulisek N, Guo X, Wu J, Vranic I, Panaccione R and Vermeire S (2024). Analysis of tofacitinib safety in ulcerative colitis from the completed global clinical developmental program up to 9.2 years of drug exposure. *United European Gastroenterol. J.*, **12**(6): 793-801.
- Ramos L, Ramos-Rodriguez J, Barreda R, Gutierrez-Nicolás F, Carrillo-Palau M, Alonso-Abreu I, Nazco-Casario J and Quintero E (2022). Adherence to subcutaneous biologic treatment for inflammatory bowel disease. *Gastroenterol. Hepatol.*, **45**(5): 335-341.
- Rutgeerts P, Sandborn WJ, Feagan BG, Reinisch W, Olson A, Johanns J, Travers S, Rachmilewitz D, Hanauer SB, Lichtenstein GR, de Villiers WJS, Present D, Sands BE and Colombel JF (2005). Infliximab for induction and maintenance therapy for ulcerative colitis. *N. Engl. J. Med.*, **353**(23): 2462-2476.
- Saadoun AA, Abdelsattar AH, Elsaid AH, Abdelaleam EA, Abdelkader HK, Ibrahim HM, Saad MS, Ellawi MS, Elsaid RE, Maghrabia A, Ibrahim D and Ramadan NM (2025). Repurposing liraglutide to the management of DSS-induced colitis: A potential for promoting autophagy. *Naunyn. Schmiedeberg's Arch. Pharmacol.*, **398**: 17173-17185.
- Safran M, Rosen N, Twik M, BarShir R, Iny Stein T, Dahary D, Fishilevich S and Lancet D (2021). The GeneCards Suite. In: Abugessaisa I and Kasukawa T (eds), Practical Guide to Life Science Databases. Springer, Singapore, pp. 27-56. doi:10.1007/978-981-16-5812-9_2.
- Sandborn WJ, D'Haens GR, Sands BE, Panaccione R, Ng SC, Lawendy N, Kulisek N, Modesto I, Guo X, Mundayat R, Su C, Vranic I and Panes J (2023). Tofacitinib for the treatment of ulcerative colitis: An integrated summary of up to 7.8 years of safety data from the global clinical programme. *J. Crohns. Colitis.*, **17**(3): 338-351.
- Sun H, Shu J, Tang J, Li Y, Qiu J, Ding Z, Xuan B, Chen M, Gan C, Lin J, Qiu J, Sheng H and Wang C (2024). GLP-1 receptor agonists alleviate colonic inflammation by modulating intestinal microbiota and the function of group 3 innate lymphoid cells. *Immunology.*, **172**(3): 451-468.
- Villumsen M, Schelde AB, Jimenez-Solem E, Jess T and Allin KH (2021). GLP-1 based therapies and disease course of inflammatory bowel disease. *E Clinical Medicine*, **37**: 100979.
- Vootukuru N and Vasudevan A (2024). Approach to loss of response to advanced therapies in inflammatory bowel disease. *World J. Gastroenterol.*, **30**(22): 2902-2919.
- Wang W, Zhang C, Zhang H, Li L, Fan T and Jin Z (2023). The alleviating effect and mechanism of GLP-1 on ulcerative colitis. *Aging (Albany NY)*, **15**(16): 8044-8060.
- Weng J and Lo CC (2025). Gut hormones and inflammatory bowel disease. *Biomolecules*, **15**(7): 1013.
- Winthrop KL, Loftus EV, Baumgart DC, Reinisch W, Nduaka CI, Lawendy N, Chan G, Mundayat R, Friedman GS, Salese L, Thorpe AJ and Su C (2021). Tofacitinib for the treatment of ulcerative colitis: Analysis of infection rates from the ulcerative colitis clinical programme. *J. Crohns. Colitis.*, **15**(6): 914-929.
- Wisniewski AFZ, Bate A, Bousquet C, Brueckner A, Candore G, Juhlin K, Macia-Martinez M, Manlik K, Quarcio N, Seabroke S, Slattery J, Southworth H, Thakrar B, Tregunno P, Van Holle L and Noren GN

- (2016). Good signal detection practices: Evidence from IMI PROTECT. *Drug Saf.*, **39**(6): 469-490.
- Yanai H, Ellul P, Verstockt B, Greuter T, Kopylov U, Casanova MJ, Dragoni G, Eder P, Estevinho MM, Abreu C, Furfaro F, Kapizioni C, Karmiris K, Katsanos K, Kirghesner J, Leshem E, Noor NM, Pellino G, Pugliese D, Toruner M, Vigeat N, Zabana Y, Zagorowicz ES and Gisbert JP (2026). ECCO guidelines on the prevention, diagnosis and management of infections in inflammatory bowel disease. *J. Crohns Colitis.*, **20**(7): jjag071.
- Yukselen Z, Raju AKV, Kumar PA, Ujjawal A, Dasari M, Parajuli S, Nakhla M, Bansal K, Ganatra S and Dani SS (2024). A real-world pharmacovigilance study of FDA adverse event reporting system (FAERS) for mavacamten. *Am. J. Cardiovasc. Drugs*, **24**(6): 791-799.
- Zhou S, Su F, Gao Q, Wang M, Duan J and Li J (2026). Cordyceps cicadae polysaccharides ameliorate ulcerative colitis by modulating the gut microbiota and regulating the bile acid/FXR/NF- κ B signaling pathway. *Phytomedicine*. **153**:158007.