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Meta-analysis review

Comparative efficacy and safety of vedolizumab and antitumor necrosis factor alfa in patients with inflammatory bowel diseases: A meta-analysis

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ABSTRACT

This meta-analysis directly compares the efficacy and safety of vedolizumab and tumor necrosis factor-α (TNF-α) inhibitors for patients with inflammatory bowel disease (IBD), contrary to the previous one which provided an indirect comparison. In this meta-analysis, only the studies that directly compared two treatments (vedolizumab and TNF-α inhibitors) to each other (head-to-head approach) were considered. A comprehensive literature search was conducted using the following databases: PubMed, Embase, the Cochrane Library, and Web of Science. The pooled estimates of efficacies and safety were calculated as relative risk (RR) and 95 % confidence interval (CI). The presence of bias in the published material was evaluated using Begg's test. Sensitivity analysis was used to evaluate the pooled results' robustness. In total, 32 eligible studies were finally included. Results showed that the efficacy of vedolizumab was superior to TNF-α inhibitors in clinical remission [1.26, 95 % CI: 1.15–1.39]. Moreover, the vedolizumab group showed a reduced incidence of severe adverse events (RR = 0.63, 95 % CI: 0.42–0.94) compared to TNF-α inhibitors. Our results revealed superior efficacy and safety of vedolizumab compared to TNF-α inhibitors, which provided direct evidence for the use of vedolizumab in IBD treatment. Future studies are needed to confirm our findings.

Keywords: vedolizumab, TNF-α inhibitors, inflammatory bowel disease, ulcerative colitis

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INTRODUCTION

Inflammatory bowel disease (IBD) is a group of gastrointestinal disorders with the principal phenotypes of ulcerative colitis (UC) and Crohn's disease (CD) (1, 2). The prevalence of IBD is estimated to be 1.5 million and 2 million cases, resp., in North America and Europe (3). The underlying mechanisms of IBD are complex, involving the interplay of genetic predisposition, environmental factors, and alterations in the intestinal microbiome, which impair intestinal barrier function and disrupt immune responses (4). Evidence has shown significant inflammatory cell infiltration in the intestinal mucosa of IBD patients (4). The activation of white blood cells in the mucosa is a key process in IBD pathogenesis, mediated by selectins, integrins, chemokine receptors, vascular cell adhesion molecule-1 (VCAM-1),

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and mucosal addressing cell adhesion molecule-1 (MAdCAM-1) (5). Tumor necrosis factor-α (TNF-α), a proinflammatory cytokine, plays a role in IBD pathogenesis (6). TNF-α inhibitors were the first class of biological agents approved for IBD treatment, effective against both luminal and extraintestinal manifestations (7). However, these inhibitors can increase susceptibility to serious infections and may lead to treatment failures, resulting in reduced drug efficacy (8, 9).

Considering that there is limited evidence regarding the comparative efficacy and safety of TNF-α inhibitors and vedolizumab in IBD, systematic reviews and meta-analyses synthesizing data pertaining to biological agents (vedolizumab and TNF-α inhibitors) were needed. A meta-analysis compared vedolizumab and TNF-α inhibitors for the treatment of IBD patients, although it did not include a direct head-to-head comparison (7). Another meta-analysis focused on comparing vedolizumab and TNF-α inhibitors specifically for treating patients with UC, without considering those with CD (5). Therefore, the current meta-analysis is performed in a head-to-head manner to comprehensively evaluate the efficacy and safety of vedolizumab and TNF-α inhibitors in patients with IBD. Further, the efficacy and safety of these biological agents were assessed in individuals with different forms of IBD.

SOURCES AND METHODS

This meta-analysis was conducted in accordance with the PRISMA guidelines (14).

Literature search strategy

Two researchers independently performed systematic searches of Embase, PubMed, Web of Science, and Cochrane Library up to November 15, 2024, for relevant studies. The search strategies are shown in Supplementary File 1. The third researcher provided the consultation if conflicts existed.

Inclusion and exclusion criteria

The inclusion criteria were: (*i*) patients – IBD patients (CD, UC, or IBD-unclassified), (*ii*) intervention – vedolizumab group, (*iii*) control – TNF-α inhibitors group (including etanercept, infliximab, adalimumab, certolizumab, or golimumab), (*iv*) outcomes – clinical remission, clinical response, steroid-free remission (SFR), endoscopic remission (ER), histologic remission (HR), endoscopic improvement (EI), treatment failure (TF; IBD-related surgery or hospitalization), adverse events (AEs, severe AEs, infections, or severe infections), (*v*) studies – cohort studies and randomized controlled trials (RCTs). Exclusion criteria: (*i*) animal studies or *in vitro* experiments, (*ii*) conference abstract, case report, meta-analysis, review, editorial materials, letters, guidelines, news items, patents, (*iii*) not published in the English language, (*iv*) articles that have been withdrawn, (*v*) topic failing to meet the requirements. Details of the definition of outcomes are attached in Supplementary File 2.

Data extraction

Two researchers independently performed the data extraction. The following characteristics were extracted from the studies: the first author, country, publication year, study

design, biological treatment, IBD subtype, sample size, sex, age, follow-up time, diagnosis age, disease duration, Mayo score, and prior biologic therapy.

Quality assessment

The Newcastle-Ottawa scale (NOS) was employed to assess cohort studies, with evaluation conducted across three dimensions (selection of study population, comparability of the groups, and outcome evaluation) (15). The studies included in the analysis were categorized based on their quality, with low-quality studies receiving scores of 1 to 3 points, moderate-quality studies scoring between 4 and 6 points, and high-quality studies achieving scores of 7 to 9 points. Higher scores represented a higher quality of studies.

The RCTs included in the meta-analysis were assessed using the Jadad scale, which was evaluated in four dimensions (generation of random sequence, randomization concealment, blinding, withdrawal, and loss of follow-up) (16, 17). Based on the Jadad scale scores, studies were categorized into low quality (1–3 points) and high quality (4–7 points), with higher scores indicating more rigorous and reliable study designs.

Statistical analysis

A pooled relative risk (RR) with a 95 % confidence interval (CI) was calculated for counting data. A heterogeneity test was conducted to assess the statistical heterogeneity across the included studies by using the I^2 statistic. The random-effects model was employed to perform meta-analyses if $I^2 \geq 50$ %, and the fixed-effects model was used if $I^2 < 50$ %. A subgroup analysis was conducted to elucidate the source of heterogeneity, based on IBD subtypes. The presence of bias in the published literature was evaluated for the outcomes using Begg's test (18). A sensitivity analysis was conducted to evaluate the reliability of the pooled results by sequentially removing the individual study. All statistical analyses were conducted using Stata15.1 software (StataCorp, College Station, TX, USA), and a *p*-value of less than 0.05 was set as statistically significant.

RESULTS AND DISCUSSION

Search results and study characteristics

Finally, 5,635 articles were included, of which, 1,930 duplicates were removed. Following an initial screening, 3,565 articles were excluded for the following reasons: topics not meeting the requirements (n = 764), reviews or meta-analyses (n = 592), not published in English (n = 6), animal experiments (n = 2), guidelines (n = 14), meeting abstracts, or case reports (n = 1,760), trial registrations records (n = 321), editorial materials, letters or retractions (n = 106). After screening the full text, 108 articles were excluded: data not available (n = 1), outcome not meeting the requirements (n = 29), duplicated subjects (n = 9), or other excluded criteria (n = 69). Finally, 32 eligible studies were included (Fig. 1) (12, 13, 19–48).

Table I shows the included studies' characteristics. There were 31 cohort studies and 1 randomized controlled trial involving 5,640 patients in the vedolizumab group and 15,480 patients in the TNF-α inhibitors group. According to the NOS scores, 19 studies met

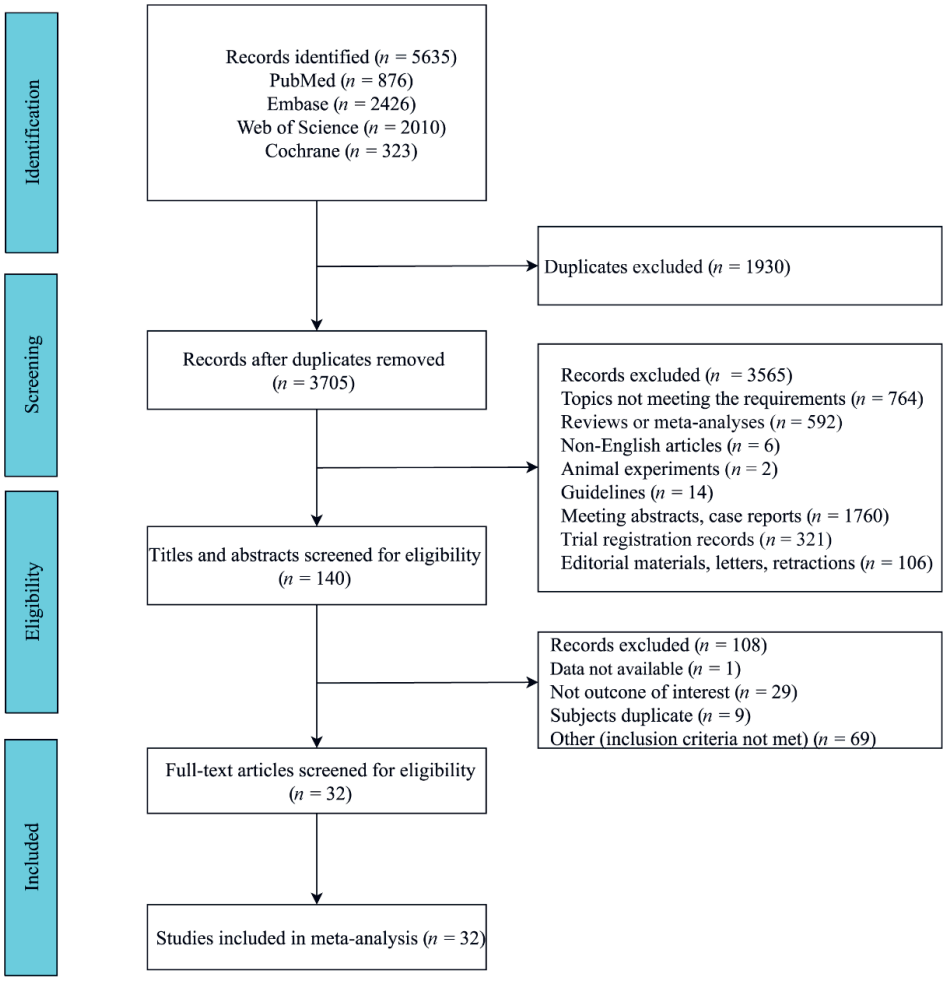

Fig. 1. The flowchart of the study search.

7–9 criteria (NOS, high quality) while the remaining 12 studies met 6 criteria (NOS, moderate quality). One RCT study obtained 6 points by Jadad scale scores and was assessed as high quality.

Pooled results for the efficacy and safety of vedolizumab and TNF-α inhibitors

Compared to TNF-α inhibitors, vedolizumab was superior in clinical remission (RR = 1.26, 95 % CI: 1.15–1.39) (Fig. 2a) for IBD patients. In terms of safety, the pooled results showed that the risk of severe AEs (RR = 0.63, 95 % CI: 0.42–0.94) (Fig. 2b) in the vedolizumab group was lower than in the TNF-α inhibitors group. No significant differences

Table I. The characteristics of the included studies

Treatment	IBD subtype	Sample size (*n*)	Age (year)	Follow-up (month)	Disease duration (year)	Quality assessment	Outcome	Reference / year	Country
Vedolizumab	CD, UC, unclassified IBD	103	68 (6)*	> 12	16 (14)*	8	CR, TF, AEs	19/2019	USA
TNF antagonists		131	68 (6)*		13 (15)*				
Vedolizumab	UC	32	54.5 (17.9)*	3.75	-	6	Clinical response	20/2018	USA
Infliximab		27	42.3 (18.5)*	3.10					
Vedolizumab	CD	659	25.59 (13.81)*	> 12	12 (13)*	6	AEs	21/2020	USA
Infliximab		305	27.8 (13.76)*		3 (10)*				
TNF antagonists		302	28.99 (14.53)*		6 (17)*				
Vedolizumab	UC	380	45.7 (17.4)*	> 24	–	6	CR, clinical response, AEs	24/2021	Canada
TNF antagonists		224	39.6 (15.7)*						
Vedolizumab	CD	218	51.7 (16.8)*						
TNF antagonists		273	39.7 (14.8)*						
Vedolizumab	UC	385	40.8 (13.7)*	17	7.3 (7.2)*	6	CR, clinical response, SFR, HR, TF, EI, AEs	44/2019	USA
Adalimumab		386	40.5 (13.4)*		6.4 (6.0)*				
Vedolizumab	UC	142	47 (16.9)*	13	10 (4,14)^	7	CR, ER, SFR, EI, AEs	25/2022	Italy
Adalimumab		90	42.6 (14.8)*		10.1 (3, 14.8)^				
Golimumab		79	42.2 (13.2)*		10.4 (2, 15)^				
Vedolizumab	UC	195	48 (33)^	19.57	7 (16)^	7	SFR	26/2023	USA
Adalimumab		278	36 (24)^	9.55	5 (9)^				
Infliximab		332	34 (25)^	15.78	3 (9)^				
Vedolizumab	UC	97	46 (32.0, 57.0)^	11.4	–	8	AEs	29/2019	Italy
Adalimumab		64	46.5 (30.0, 56.0)^						

Treatment	IBD subtype	Sample size (*n*)	Age (year)	Follow-up (month)	Disease duration (year)	Quality assessment	Outcome	Reference / year	Country
Vedolizumab	UC	39	–	–	–	8	AEs	30/2021	Canada
Adalimumab		58							
Infliximab		68							
Vedolizumab	CD, UC	23	–	> 18	–	7	CR, clinical response	12/2022	Brazil
Adalimumab		57							
Infliximab		42							
Vedolizumab	UC	71	43 (17.3)*	21	9.09	6	CR, clinical response, AEs	32/2020	France
Infliximab		154	42.5 (16.6)*	33	6.38				
Vedolizumab	CD, UC	85	–	–	–	7	AEs	33/2021	Italy
TNF antagonists		447							
Vedolizumab	CD, UC	377	–	7.6	12.0 (10.5)*	8	TF, AEs	46/2022	USA
TNF antagonists		377		7.6	12.5 (10.2)*				
Vedolizumab	UC	103	44.4 (15.7)*	> 12	1.9 (1.1)*	6	TF	35/2020	USA
Adalimumab		1291	44.8 (14.4)*		1.4 (1.0)*				
Infliximab		810	43.8 (15.8)*		1.3 (1.1)*				
Golimumab		127	45.3 (15.2)*		1.5 (0.9)*				
Vedolizumab	UC	454	42.08 (17.13)*	11.1	6 (11)*	6	CR, SFR, AEs	36/2020	USA
Infliximab		165	38.47 (15.97)*		3 (6)*				
TNF antagonists		103	40.11 (15.28)*		6 (11)*				
Vedolizumab	UC	187	55.0 (40.3, 66.9)^	11.9	9.3 (4.0, 16.0)^	6	CR, SFR	37/2020	Italy
Adalimumab		168	42.0 (33.0, 53.8)^		8.0 (3.0, 14.1)^				
Golimumab		108	49.0 (39.0, 56.10)^		9.5 (4.0, 16.0)^				

Treatment	IBD subtype	Sample size (*n*)	Age (year)	Follow-up (month)	Disease duration (year)	Quality assessment	Outcome	Reference / year	Country
Vedolizumab	CD	277	52.0 (37.0, 64.0)^	14	10.0 (6.0,18.0)^	6	CR, SFR	38/2021	Italy
Adalimumab	UC	308	40.8 (28.5, 52.7)^		6.0 (2.0, 12.0)^				
Vedolizumab	UC	63	–	13	5 (1,11)^	7	CR, ER, SFR, EI, AEs	40/2022	Belgium
Adalimumab		46			3.5 (1,7.5)^				
Vedolizumab	CD	33			4 (1, 11)^				
Adalimumab		53			3 (0,17)^				
Vedolizumab	CD, UC, unclassified IBD	108	–	15.24	15.5 (5. 0,30)^	7	ER, HR	41/2022	USA
TNF antagonists		104		17.16	10 (2, 25)^				
Vedolizumab	UC, CD	542	51.4 (16.6)*	–	4.31	8	TF	42/2019	Canada
Infliximab		1179	51.4 (16.6)*						
Vedolizumab	UC	42	44.9 (19.2)*	12	–	6	CR, clinical response, SFR	28/2019	UK
TNF antagonists		97	40.4 (17.3)*						
Vedolizumab	CD, UC	73	61.0 (16.9)*	18	–	7	AEs	43/2020	Italy
Infliximab		308	42.0 (14.7)*	21.1					
Adalimumab		215	44.1 (14.3)*	19					
Golimumab		26	48.1 (14.5)*	19.3					
Vedolizumab	UC	32	–	11.25	8 (8.56)*	6	CR, clinical response, SFR, AEs	13/2023	Italy
Infliximab		50		9.25	9.5 (9.29)*				
Vedolizumab	CD, UC	17	52.5 (15.5)*	–	–	7	AEs	47/2022	Italy
Infliximab		214	42.5 (14.1)*						
Golimumab		37	42.6 (13.3)*						
Adalimumab		89	42.2 (14.0)*						

Treatment	IBD subtype	Sample size (*n*)	Age (year)	Follow-up (month)	Disease duration (year)	Quality assessment	Outcome	Reference / year	Country
Vedolizumab	CD	86	39.8 (29.3–53.9)^	79.2	2	7	CR, clinical response, SFR, AEs	22/2024	Germany
TNF antagonists		241	40.7 (29.4–54.8)^	54					
Vedolizumab	UC	182	39.6 (28.3–53.2)^	57.6	2	6	CR, clinical response, SFR, AEs	23/2023	Germany
TNF Antagonists		132	39.6 (28.3–53.2)^	52.8					
Vedolizumab	CD, UC	73	43.9 (15.0)*	144	⩾1	8	CR, ER, TF	27/2024	Italy
infliximab		158							
Vedolizumab	UC	117	40.7 (15.3)*	53.7	4.3	7	CR, clinical response, ER, SFR, AEs	31/2024	China
infliximab		82	41.1 (14.6)*	59.9					
Vedolizumab	CD, UC	284	27 (21–41)^	–	1.55 (1.05)*	7	AEs	34/2024	Korea
TNF antagonists		4902							
Vedolizumab	UC	57	49 (33–56)^	36	4.3	8	CR, ER, SFR, AEs	39/2024	China
infliximab		65	41 (29–49)^	24					
Vedolizumab	CD, UC	53	34.12 (10.66)*	–	4.3	6	ER, SFR, TF	45/2024	Kuwait
TNF antagonists		294							
Vedolizumab	CD, UC	51	–	–	2.38	7	CR, ER, SFR	48/2024	Germany
TNF antagonists		414							

AEs – adverse events, EI – endoscopic improvement, CD – Crohn's disease, CR – clinical remission, ER – endoscopic remission, HR – histologic remission, RCT – randomized controlled trial, SFR – steroid-free remission, TF – treatment failure, TNF – tumour necrosis factor, UC – ulcerative colitis

* – mean (SD), ** – median (IQR), ^ – median (Q1, Q3)

Table II. Pooled results for efficacy and safety of vedolizumab vs. *TNF-α inhibitors in IBD patients*

Outcome	Number of studies	RR (95 % CI)	*p*	I^2
Clinical remission				
Overall	16	1.26 (1.15, 1.39)	< 0.001	52.9
Sensitivity analysis		1.26 (1.15, 1.39)		
Clinical response				
Overall	11	1.10 (0.99, 1.22)	0.090	83.5
Sensitivity analysis		1.10 (0.99, 1.22)		
ER				
Overall	8	1.10 (0.87, 139)	0.449	55.3
Sensitivity analysis		1.10 (0.87, 1.39)		
SFR				
Overall	14	1.16 (0.99, 1.36)	0.072	76.6
Sensitivity analysis		1.16 (0.99, 1.36)		
HR				
Overall	2	1.75 (0.51, 5.93)	0.372	91.7
Sensitivity analysis		1.75 (0.51, 5.93)		
EI				
Overall	3	1.18 (0.86, 1.63)	0.309	77.4
Sensitivity analysis		1.18 (0.86, 1.63)		
IBD-related surgery				
Overall	4	1.30 (1.04, 1.63)	0.024	46.3
Sensitivity analysis		1.30 (1.04, 1.63)		
IBD-related hospitalization				
Overall	6	0.96 (0.82, 1.13)	0.625	46.5
Sensitivity analysis		0.96 (0.82, 1.13)		
AEs				
Overall	13	0.81 (0.65, 1.01)	0.057	52.6
Sensitivity analysis		0.81 (0.65, 1.01)		
Severe AEs				
Overall	5	0.63 (0.42, 0.94)	0.023	71.6
Sensitivity analysis		0.63 (0.42, 0.94)		
Infection				
Overall	4	0.92 (0.66, 1.27)	0.595	0.0
Sensitivity analysis		0.92 (0.66, 1.27)		
Severe infection				
Overall	5	0.83 (0.49, 1.40)	0.479	67.6
Sensitivity analysis		0.83 (0.49, 1.40)		

AEs – adverse events, CI – confidence interval, EI – endoscopic improvement, ER – endoscopic remission, HR – histologic remission, I^2 – I-squared statistic, IBD – inflammatory bowel disease, RR – relative risk, SFR – steroid-free remission, TF – treatment failure, TNF – tumour necrosis factor

were observed in clinical response, ER, SFR, HR, EI, IBD-related hospitalization, AEs, infection, and severe infection between the vedolizumab group and TNF-α inhibitors group (Table II).

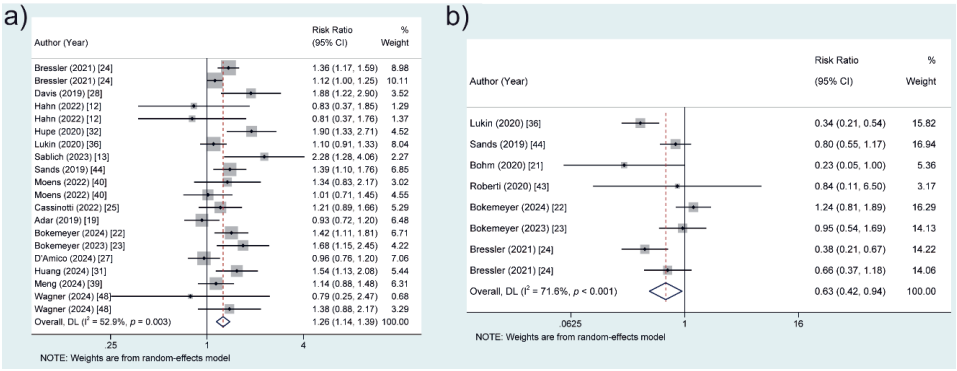

Fig. 2. Forest plots of vedolizumab *vs.* TNF-α inhibitors for the efficacy and safety of treating patients with IBD: a) clinical remission, b) severe AEs.

AEs – adverse events, IBD – inflammatory bowel disease, TNF – tumor necrosis factor

Subgroup assessment

Table III summarizes the efficacy and safety of vedolizumab and TNF-α inhibitors according to different types of IBD. We also found the superior efficacy of vedolizumab to TNF-α inhibitors in clinical remission (RR = 1.38, 95 % CI: 1.24–1.55), clinical response (RR = 1.19, 95 % CI: 1.05–1.34), SFR (RR = 1.21, 95 % CI: 1.02–1.43) for UC patients. A superior clinical remission (RR = 1.16, 95 % CI: 1.02–1.31) of vedolizumab (*vs.* TNF-α inhibitors) was also observed in CD patients. Compared to the TNF-α inhibitors, vedolizumab was associated with decreased AEs (RR = 0.70, 95 % CI: 0.54–0.92) and severe AEs (RR = 0.56, 95 % CI: 0.34–0.93) in UC patients.

Sensitivity analysis and publication bias

Sensitivity analysis demonstrated that the estimates did not significantly vary when omitting studies one by one (Table II). Publication bias was deemed not to be significant for clinical remission (Z = 1.01, p = 0.327), clinical response (Z = 0.82, p = 0.429), SFR (Z = 1.28, p = 0.219), and AEs (Z = –1.72, p = 0.111) (Table IV).

In the current meta-analysis with 32 studies, vedolizumab yielded better efficacy (clinical remission) and safety (severe AEs) than TNF-α inhibitors in IBD patients. Especially in UC patients, vedolizumab may achieve better performance in clinical remission, clinical response, SFR, AEs, and severe AEs.

Implications of the outcomes

TNF-α inhibitors are widely used biological agents in the clinical treatment of IBD and can be capable of neutralizing TNF-α (6). A meta-analysis suggested that TNF⊚α inhibitors monotherapy or combined therapy was the preferred strategy for mucosal healing in IBD compared to conventional treatments such as glucocorticoids, immunosuppressants, and salicylic acid formulations (49). Vedolizumab was a selective treatment of IBD

Table III. Pooled results for efficacy and safety of vedolizumab vs. *TNF-α inhibitors in IBD subtypes*

Outcomes	Number of studies	RR (95 % CI)	*p*	I^2
Clinical remission				
UC	13	1.38 (1.24, 1.55)	< 0.001	38.0
CD	5	1.16 (1.02, 1.31)	0.029	14.1
Clinical response				
UC	10	1.19 (1.05, 1.34)	0.005	79.3
CD	4	0.92 (0.70, 1.19)	0.510	90.2
ER				
UC	6	1.24 (0.87, 1.77)	0.239	61.2
CD	3	0.88 (0.67, 1.16)	0.353	0.0
SFR				
UC	13	1.21 (1.02, 1.43)	0.033	64.9
CD	5	1.08 (0.78, 1.49)	0.645	84.6
EI				
UC	3	1.28 (0.82, 2.00)	0.279	79.4
CD	1	0.98 (0.77, 1.25)	0.865	0.0
IBD-related surgery				
UC	3	1.56 (1.07, 2.26)	0.020	59.0
CD	3	1.21 (0.89, 1.64)	0.234	56.7
IBD-related hospitalization				
UC	4	0.98 (0.77, 1.26)	0.883	73.6
CD	3	1.00 (0.80, 1.26)	0.980	0.0
AEs				
UC	10	0.70 (0.54, 0.92)	0.010	49.1
CD	2	1.32 (0.99, 1.76)	0.059	0.0
Severe AEs				
UC	4	0.56 (0.34, 0.93)	0.025	76.9
CD	3	0.73 (0.36, 1.51)	0.396	69.4
Severe infections				
UC	3	0.64 (0.37, 1.11)	0.110	37.5
CD	2	0.83 (0.38, 1.80)	0.639	24.6

AEs – adverse events, EI – endoscopic improvement, CI – confidence interval, ER – endoscopic remission, HR – histologic remission, I^2 – I-squared statistic, IBD – inflammatory bowel disease, RR – relative risk, SFR – steroid-free remission, TF – treatment failure, TNF – tumor necrosis factor, UC – ulcerative colitis

Table IV. Publication bias of outcomes by Begg's test

Outcomes	Begg's test	
	Z	*p*
Clinical remission	1.01	0.327
Clinical response	0.82	0.429
SFR	1.28	0.219
AEs	–1.72	0.111

AEs – adverse events, SFR – steroid-free remission

by blocking white blood cell transport to the intestines (50). TNF-α inhibitors and vedolizumab can both effectively induce and maintain mucosal healing, and have become the first-line biological agents for the treatment of IBD (12). A previous meta-analysis that included 14 studies on IBD demonstrated similar results in the efficacy and safety profiles of infliximab and vedolizumab by comparing the occurrence rates of various outcome measures (7). A study by Cholapranee *et al*. (51) reports that both anti-TNF and anti-integrin biologics (vedolizumab) effectively induced mucosal healing in UC patients compared to placebo. A network meta-analysis ranked infliximab and vedolizumab highest among first-line treatments for inducing remission and mucosal healing in moderate-to-severe UC, based on indirect comparisons (52). Additionally, a head-to-head randomized trial demonstrated that vedolizumab was more effective than adalimumab in achieving clinical response and remission during both induction and maintenance therapy, while also providing a favorable balance of efficacy and safety compared to other available UC treatments (53). Consistently, our meta-analysis showed that vedolizumab exerted a better effect on clinical remission than TNF-α inhibitors in IBD patients.

Some IBD patients may demonstrate a lack of response or a reduction in response to TNF-α inhibitors, which are also linked to higher risks of infections and malignancies (54). Different from TNF-α inhibitors, vedolizumab inhibits the interaction between white blood cells and the intestinal vascular system by blocking the binding of integrin and MAdCAM-1 on intestinal endothelial cells to accurately and selectively suppress intestinal inflammation without any adverse effects of systemic immune suppression (5). Our results indicated that the risk of severe AEs of vedolizumab was lower than that of TNF-α inhibitors in IBD patients. This may be explained by the intestinal selective effect of vedolizumab, which did not affect the body's immune function, thereby increasing safety. Further, we found that the efficacy and safety of vedolizumab were superior to TNF-α inhibitors regarding clinical response, SFR, AEs, and severe AEs in patients with UC while not in patients with CD. This finding indicated that vedolizumab may be more suitable for UC patients, and the efficacy and safety of vedolizumab needed to be further explored in CD patients.

While discussing, we highlight that although vedolizumab and TNF-α inhibitors have shown positive efficacy in many patients with IBD, a subset of patients are insensitive to or do not respond well to these treatments. Therefore, the exploration of novel therapeutic approaches is critical for these nonresponsive patients. In recent years, Janus kinase 1 (JAK1) inhibitors such as tofacitinib, filgotinib, upadacitinib, *etc*. (55), and sphingosine

1-phosphate (S1P) receptor modulators, such as etrasimod (56), have shown promising clinical effects, providing new options for patients with refractory IBD. In addition, biological agents targeting IL-23/12, such as ustekinumab and mirikizumab (57), are also in clinical use, and these agents target different inflammatory pathways through different mechanisms, which may open up new therapeutic prospects for patients who have failed to benefit from traditional therapies. Therefore, future studies need to focus on the long--term efficacy and safety of these new therapies in order to provide a more comprehensive treatment strategy for IBD patients.

Limitations of the study

However, it should be noted that this meta-analysis is not without limitations. First, only studies published in the English language were included, and it may lead to a bias related to language. Secondly, while our subgroup analyses were performed based on different subtypes of IBD, we observed that some outcomes still exhibited heterogeneity. Additionally, prior biologic therapy and variations in treatment protocols may influence the assessment of both efficacy and safety of the treatments. However, due to limitations in the original studies, we are unable to conduct further analyses to explore these factors in more depth. Third, the included studies are all performed in Europe and America. It is not possible to generalize the findings to patients living in other areas. In the future, more RCTs need to be performed to further explore this in patients from the other areas.

CONCLUSIONS

We explored the efficacy and safety of vedolizumab and TNF-α inhibitors in patients with IBD based on currently available studies. The present meta-analysis provided evidence that vedolizumab could be a preferred treatment option that combines both efficacy and safety for patients with IBD, particularly in those with UC. These results highlight the potential of vedolizumab as a targeted therapy that may reduce the systemic side effects associated with traditional TNF-α inhibitors. Our findings provide direct evidence for the use of vedolizumab in the treatment of IBD. Future large RCTs with robust designs and multicenter involvement are essential to further validate these findings and explore optimal treatment protocols.

Supplementary materials are available upon request.

Acronyms, abbreviations, codes. – AEs – adverse events, $\alpha4\beta7$ – alpha4beta7, CD – Crohn's disease, EI – endoscopic improvement, ER – endoscopic remission, HR – histologic remission, IBD – inflammatory bowel disease, MAdCAM-1 – mucosal addressing cell adhesion molecule-1, NOS – Newcastle-Ottawa scale, RCTs – randomized controlled trials, RR – relative risk, S1P – sphingosine 1-phosphate, SFR – steroid-free remission, TF – treatment failure, TNF-α – tumor necrosis factor-α, UC – ulcerative colitis, VCAM-1 – vascular cell adhesion molecule-1.

Conflict of interests. – The authors declare no competing interests.

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