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CLINICAL OUTCOMES OF ANTI-TNF AGENTS COMPARED TO VEDOLIZUMAB AMONG ADULT PATIENTS DIAGNOSED WITH CROHN'S DISEASE: A SYSTEMATIC REVIEW

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ABSTRACT

Introduction: Crohn's disease (CD) is a chronic inflammatory bowel disease characterized by transmural inflammation and granuloma formation. Biologic agents, including Anti-TNF agents (Infliximab, Adalimumab) and Vedolizumab, have revolutionized the management of CD by targeting key inflammatory pathways. This systematic review aims to evaluate the efficacy and safety of these agents in adult patients with CD. **Methods:** A comprehensive search was conducted in databases and registers, including PubMed, Embase, Cochrane Library, and ClinicalTrials.gov. Eligible studies investigating the efficacy and safety of Anti-TNF agents and Vedolizumab in CD patients were included. Data were extracted and synthesized narratively. **Results:** The included studies demonstrated the effectiveness of Anti-TNF agents in inducing and maintaining remission in CD patients. Infliximab and Adalimumab showed significant clinical response rates, with 70-point response rates ranging from 34% to 52% at week 4. Vedolizumab, an integrin receptor antagonist, also exhibited promising results. Among CD patients who had failed previous Anti-TNF therapy, Vedolizumab demonstrated remission rates of 15.2% at week 6 and 26.6% at week 10, compared to placebo rates of 12.1% and 12.1%, respectively. Additionally, Vedolizumab was associated with a higher CDAI-100 response rate of 39.2% at week 6, compared to 22.3% with placebo. **Conclusion:** Both Anti-TNF agents and Vedolizumab have shown efficacy in the treatment of CD. Anti-TNF agents demonstrated significant clinical response rates and remission induction. Vedolizumab provided a viable treatment option for CD patients who had failed previous Anti-TNF therapy, with higher remission rates observed at week 6 and week 10. Individualized treatment selection and therapeutic drug monitoring may optimize outcomes. However, careful monitoring and management of adverse events, including infections and infusion reactions, are crucial. Further research is needed to explore comparative effectiveness, long-term outcomes, and the potential role of combination therapies in CD management.

KEYWORDS: Crohn's disease, inflammatory bowel disease, biologic agents, Anti-TNF agents, Infliximab, Adalimumab, Vedolizumab, therapeutic drug monitoring, clinical remission, safety.

INTRODUCTION

Crohn's disease (CD) is a chronic, relapsing inflammatory bowel disease characterized by transmural inflammation and granuloma formation.[1] It is a complex disorder that can affect any part of the gastrointestinal tract, from the mouth to the anus. CD is associated with a wide range of symptoms, including abdominal pain, diarrhea, weight loss, and fatigue. The disease has a significant impact on the quality of life of affected individuals, leading to hospitalizations, surgeries, and long-term disability.[2] The exact cause of CD remains unclear, but it is believed to involve a combination of genetic, environmental, and immunological factors. Genetic susceptibility, alterations in the gut microbiota, dysregulation of the immune system, and an abnormal response to gut microbes are thought to play important roles in the development and progression of CD.[3] The management of CD aims to control symptoms, induce and maintain remission, and prevent complications. Treatment approaches include pharmacological therapies, lifestyle modifications, and surgical interventions.

Despite advances in the understanding of its pathophysiology, the etiology of CD remains elusive, making the management and treatment of the disease challenging. Standard treatments for CD range from anti-inflammatory drugs, immunosuppressants, to biologic agents such as tumor necrosis factor (TNF) inhibitors.[2] Among biologic agents, Anti-TNF agents such as Infliximab and Adalimumab have been extensively studied and utilized in clinical practice due to their efficacy in inducing and maintaining remission in CD.[4] However, approximately one-third of patients do not respond to anti-TNF therapy, and another third lose response over time, leading to the need for alternative treatments.[4] Vedolizumab, an integrin receptor antagonist, is one such alternative that has shown promising results in several trials, particularly among patients with previous TNF antagonist failure.[5] Vedolizumab works by selectively inhibiting leukocyte adhesion and migration into the gut, thereby reducing inflammation.[6] Preliminary studies have reported that vedolizumab is effective in inducing and maintaining remission in CD.[7]

A comprehensive analysis of the efficacy and safety of anti-TNF agents and vedolizumab for the treatment of CD is yet to be established, and there remains a need for a systematic review of existing clinical trials. Therefore, the aim of this systematic review is to critically evaluate and compare the clinical remission rates and side-effect profiles of Anti-TNF agents (Infliximab, Adalimumab) and Vedolizumab in adult patients diagnosed with Crohn's disease. By synthesizing the available evidence, this review aims to provide a comprehensive overview of the comparative effectiveness and safety of these biologic agents. The findings of this review will be valuable for healthcare professionals in making informed treatment decisions and for guiding future research in the field of CD management.

METHODS

Eligibility Criteria

- **Population**: Our inclusion criteria covered studies involving adult patients (18 years or older) who were diagnosed with Crohn's disease.
- **Intervention**: Studies that investigated the use of anti-TNF agents (Infliximab, Adalimumab) and/or Vedolizumab (an integrin receptor antagonist) in the treatment of Crohn's disease were included.
- **Comparators**: Studies where these treatments were compared against a placebo or standard care were included.
- **Outcome**: Studies that reported on the rates of clinical remission and side-effect profiles were included.
- **Study Design**: Both randomized controlled trials (RCTs) and post-hoc analysis of RCTs were included.

Information Sources

An electronic search was performed on the following databases: PubMed, Embase, Cochrane Library, and Web of Science. In order to ensure a comprehensive search, a manual search was also conducted within relevant journals and conference proceedings. The search was limited to studies conducted on human subjects and published in English.

Search Strategy

Our search strategy comprised relevant keywords such as "anti-TNF agents", "Infliximab", "Adalimumab", "vedolizumab", "Crohn's disease", and other related terms. A combination of Medical Subject Headings (MeSH) and free-text terms were used to ensure a comprehensive search. The search was conducted until June 2023.

Study Selection

Two independent reviewers screened the titles and abstracts of the identified studies for eligibility. Full-text articles were then scrutinized for inclusion based on the eligibility criteria. Studies were included if they involved adult patients (18 years or older) diagnosed with Crohn's disease, investigated the use of anti-TNF agents or vedolizumab for the treatment of Crohn's disease, compared these treatments against placebo or standard care, and reported on the rates of clinical remission and side-effect profiles. Studies that did not meet these criteria were excluded.

Data Extraction and Synthesis

A narrative synthesis was conducted. Data from the included studies were extracted, summarized, and analyzed to evaluate the efficacy and safety of anti-TNF agents and vedolizumab for the treatment of Crohn's disease. The results of the studies were reported descriptively, detailing the strengths and weaknesses of

each study. Finally, the findings were summarized, providing implications for clinical practice and potential directions for future research.

RESULTS

Of 173 studies identified, 8 duplicates were removed before screening. A total of 165 studies were screened for titles and abstracts, of which 142 were excluded as they did not meet the inclusion criteria; 23 studies were fully reviewed. A final of 10 studies were included in the systematic review. The PRISMA flowchart is depicted in Figure 1.

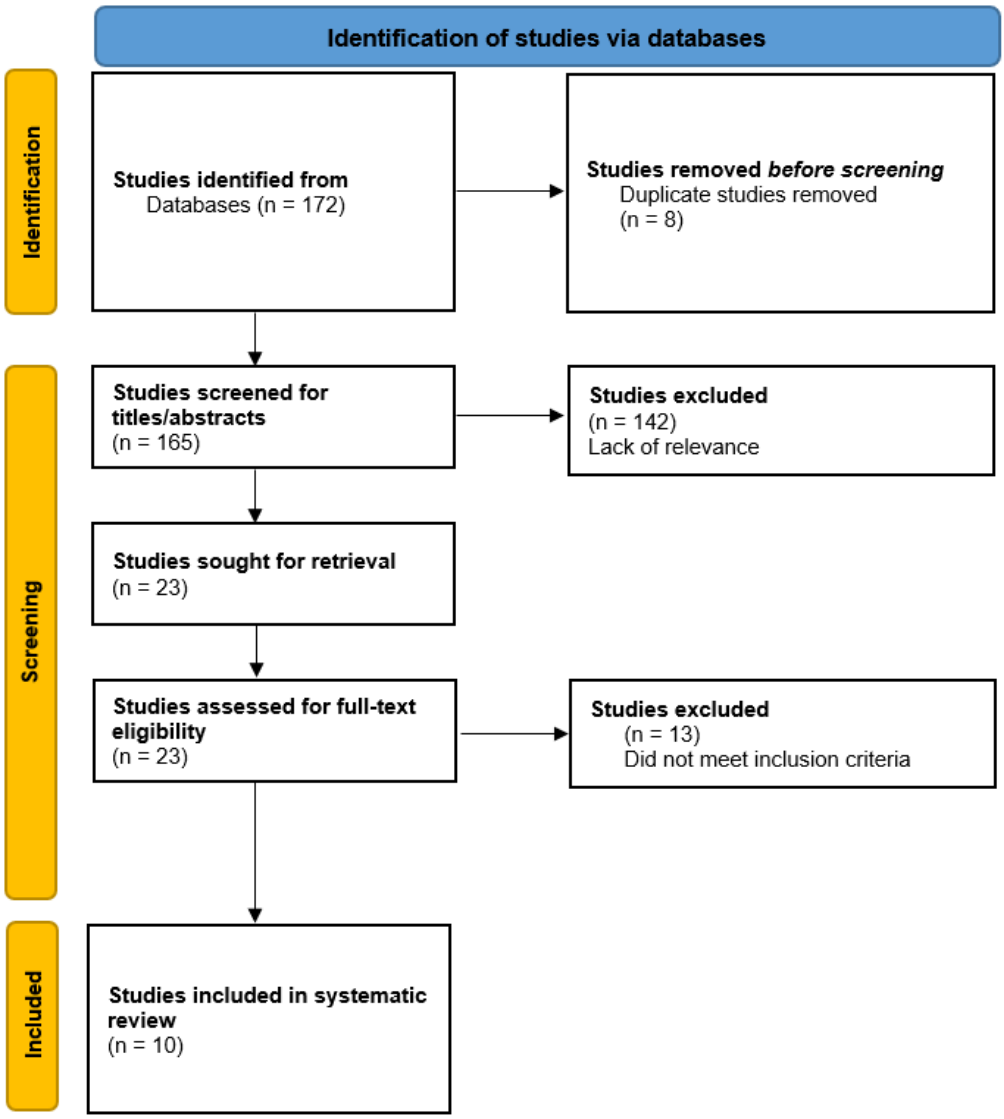

Figure 1: PRISMA flowchart depicting the study selection process.

The characteristics of included anti-TNF agent trials are enlisted in Table 1.

Table 1: Characteristics of included anti-TNF agent trials.

Identifier	Title	Study Type	Intervention	Inclusion Criteria	Primary Outcomes	N	Findings	Adverse Events
Syversen et al., 2021[8]	Effect of Therapeutic Drug Monitoring vs Standard Therapy During Infliximab Induction on Disease Remission in Patients With Chronic Immune-Mediated Inflammatory Diseases: A Randomized Clinical Trial	Randomized, parallel-group, open-label clinical trial	Proactive therapeutic drug monitoring with dose and interval adjustments (Infliximab)	Adults with rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, ulcerative colitis, Crohn disease, or psoriasis initiating infliximab therapy	Clinical remission at week 30	411 randomized patients (207 in TDM group; 204 in standard therapy group)	No significant difference in clinical remission rates between TDM and standard therapy groups (50.5% in TDM group vs. 53.0% in standard therapy group)	Adverse events were reported in 135 patients (68%) in the TDM group and 139 patients (70%) in the standard therapy group
Epelboym et al., 2017[9]	Crohn Disease: FDG PET/CT Before and After Initial Dose of Anti-Tumor Necrosis Factor Therapy to Predict Long-term Response	Prospective pilot trial	FDG PET/CT activity assessment before and 2 weeks after initiation of anti-TNF therapy (infliximab or adalimumab)	Adult patients with active Crohn disease	Clinical response, steroid-free remission, and changes in C-reactive protein (CRP) during a 12-month follow-up period	8 patients	7 out of 8 patients showed FDG activity decline at 2 weeks, 5 of whom achieved a clinical response and steroid-free remission at 8, 26, and 52 weeks. The remaining 2 patients with FDG activity decline did not achieve a clinical response or steroid-free remission at these time points, but there were reductions in CRP. The 1 patient without FDG activity decline was a clinical non-responder.	None reported
Sandborn et al., 2007[10]	Adalimumab induction therapy for Crohn disease previously treated with infliximab: a randomized trial	4-week, randomized, double-blind, placebo-controlled trial	Adalimumab (160 mg and 80 mg) at weeks 0 and 2	Adults 18 to 75 years of age with a history of moderate to severe Crohn disease for 4 months or more (Crohn's Disease Activity Index [CDAI] score, 220 to 450 points)	Induction of remission at week 4, Decreases in CDAI score by 70 or more and 100 or more points	325 adults (159 in the adalimumab group; 166 in the placebo group)	Adalimumab induced remission more frequently than placebo at week 4 (21% in adalimumab group vs. 7% in placebo group). A 70-point response occurred at week 4 in 52% of patients in the adalimumab group versus 34% of patients in the placebo group.	Two patients in the adalimumab group and 4 patients in the placebo group discontinued treatment because of adverse events. No patients in the adalimumab group and 4 patients in the placebo group had

								a serious infection.
Park et al., 2023[11]	Early Infliximab Trough Levels Predict the Long-term Efficacy of Infliximab in a Randomized Controlled Trial in Patients with Active Crohn's Disease Comparing, between CT-P13 and Originator Infliximab	Randomized, Double-Blind, Parallel-Group, Phase 3 Study (Post-Hoc Analysis)	CT-P13 (biosimilar infliximab) versus originator infliximab	Adults diagnosed with mild to moderate Crohn's disease (defined by a CDAI score of 220 and 450)	Serum infliximab trough levels at weeks 6 and 14, clinical remission at weeks 30 and 54, endoscopic remission at week 54	198 patients (100 in CT-P13 group; 98 in originator infliximab group)	The median infliximab trough levels were not different between CT-P13 and originator infliximab groups. Infliximab concentration threshold of 4.5 μg/mL at week 6 and 4.0 μg/mL at week 14 was highly predictive for long-term clinical outcomes. The combinations of clinical remission or C-reactive protein normalization with an early infliximab trough level improved the prediction of long-term clinical or endoscopic remission.	Serious adverse events were more common in the placebo group (5%) than in the adalimumab group (1%), with a rate difference of -3.5 percentage points.
Tursi et al., 2010[12]	Safety and effectiveness of infliximab for inflammatory bowel diseases in clinical practice	Clinical trial	Infliximab treatment	Patients affected by Ulcerative Colitis or Crohn's Disease	Remission status, mean Crohn Disease Activity Index (CDAI), Inflammatory Bowel Disease Quality of Life (IBDQL), Mean Disease Activity Index (DAI), Mean Mayo Subscore for Endoscopy	62 patients	84.61% of CD patients and 86.95% of UC patients achieved remission. Significant improvement in CDAI, IBDQL, DAI, and Mayo Subscore for Endoscopy observed.	8.06% of patients experienced side-effects.

Abbreviations: TDM: Therapeutic Drug Monitoring; FDG PET/CT: Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography; anti-TNF: Anti-Tumor Necrosis Factor; CRP: C-reactive protein; CDAI: Crohn's Disease Activity Index; UC: Ulcerative Colitis; CD: Crohn's Disease; IBD: Inflammatory Bowel Disease; IBDQL: Inflammatory Bowel Disease Quality of Life; DAI: Disease Activity Index

Syversen et al., 2021 conducted a randomized, parallel-group, open-label clinical trial where they used proactive therapeutic drug monitoring with dose and interval adjustments (Infliximab) on 411 randomized patients.[8] They found no significant difference in clinical remission rates between therapeutic drug monitoring and standard therapy groups, with 50.5% in the therapeutic drug monitoring group versus 53.0% in the standard therapy group. Adverse events were reported in 68% of the therapeutic drug monitoring group and 70% of the standard therapy group.

Epelboym et al., 2017 conducted a prospective pilot trial on eight patients using FDG PET/CT activity assessment before and two weeks after the initiation of anti-TNF therapy (infliximab or adalimumab).[9] They reported that 7 out of 8 patients showed FDG activity decline at 2 weeks, 5 of whom achieved a clinical response and steroid-free remission at 8, 26, and 52 weeks. The remaining two patients with FDG activity decline did not achieve a clinical response or steroid-free remission at these time points, but there were reductions in CRP. The one patient without FDG activity decline was a clinical non-responder.

Sandborn et al., 2007, in a 4-week, randomized, double-blind, placebo-controlled trial with 325 adults, reported that Adalimumab induced remission more frequently than placebo at week 4 (21% in the Adalimumab group vs. 7% in the placebo group).[10] A 70-point response occurred at week 4 in 52% of patients in the adalimumab group versus 34% of patients in the placebo group. Adverse events led to treatment discontinuation in two patients from the adalimumab group and four patients from the placebo group.

Park et al., 2023, conducted a post-hoc analysis of a randomized, double-blind, parallel-group, phase 3 study comparing CT-P13 (biosimilar infliximab) versus originator infliximab in 198 patients.[11] They found that the median infliximab trough levels were not different between the CT-P13 and originator infliximab groups. They found an infliximab concentration threshold of 4.5 μg/mL at week 6 and 4.0 μg/mL at week 14 was highly predictive for long-term clinical outcomes. The combinations of clinical remission or C-reactive protein normalization with an early infliximab trough level improved the prediction of long-term clinical or endoscopic remission. Serious adverse events were more common in the placebo group.

Tursi et al., 2010, in a clinical trial of 62 patients affected by Ulcerative Colitis or Crohn's Disease treated with infliximab, found that 84.61% of CD patients and 86.95% of UC patients achieved remission.[12] A significant improvement in CDAI, IBDQL, DAI, and Mayo Subscore for Endoscopy was observed. However, 8.06% of patients experienced side-effects.

The characteristics of included anti-TNF agent trials are enlisted in Table 2.

Table 2: Characteristics of included Vedolizumab trials.

Identifier	Title	Study Type	Intervention	Inclusion Criteria	Primary Outcomes	N	Findings	Adverse Events
Banerjee et al., 2021[13]	Efficacy and safety of vedolizumab in Crohn's disease in patients from Asian countries in the GEMINI 2 study	Phase 3, Randomized, Placebo-Controlled Trial (Post-Hoc Analysis)	Vedolizumab	Patients from Asian countries with moderate-to-severely active Crohn's disease (CD)	Clinical remission, enhanced clinical response, and change in C-reactive protein at 6 weeks; Clinical remission, enhanced clinical response, glucocorticoid-free remission and durable clinical remission at 52 weeks	Asian Countries: 51; Non-Asian Countries: 317	During induction phase, 14.7% of vedolizumab-treated patients in Asian countries achieved clinical remission at week 6 vs none with placebo. During maintenance, remission rates at 52 weeks with vedolizumab every 4 weeks, every 8 weeks and placebo were 41.7%, 36.4%, and 0% respectively. Enhanced clinical response rates were 41.7%, 63.6%, and 42.9% respectively.	39.7% of patients with vedolizumab experienced an adverse event during induction, compared to 58.8% of patients with placebo. Vedolizumab was generally well-tolerated.
Feagan et al., 2008[14]	Treatment of active Crohn's disease with MLN0002, a humanized antibody to the alpha4beta7 integrin	Randomized, double-blind, controlled trial	MLN0002 (a monoclonal antibody targeting the alpha4beta7 integrin)	Patients with active Crohn's disease	Clinical response (>or=70-point decrement in the Crohn's Disease Activity Index [CDAI] score) on day 57	MLN0002 2.0 mg/kg: 65; MLN0002 0.5 mg/kg: 62; Placebo: 58	Clinical response rates at day 57 were 53%, 49%, and 41% in the MLN0002 2.0 mg/kg, MLN0002 0.5 mg/kg, and placebo groups. Clinical remission rates at day 57 were 37%, 30%, and 21%, respectively (P = .04 for the 2.0 mg/kg vs placebo comparison).	At day 57, 12% and 34% of patients in the 2.0- and 0.5-mg/kg groups had clinically significant human anti-human antibody levels (titers > 1:125). There was one infusion-related hypersensitivity reaction. The most common serious adverse event was worsening of Crohn's disease
Sandborn et al., 2013[15]	Vedolizumab as induction and maintenance therapy for Crohn's disease	Integrated study with separate induction and maintenance trials	Vedolizumab (300 mg, intravenous)	Adults with active Crohn's disease	Clinical remission (score on the Crohn's Disease Activity Index [CDAI] of ≤150) and CDAI-100 response (≥100-point decrease in the CDAI score) at week 6 and	Induction trial: 1115 (Vedolizumab: 368, Placebo: 747); Maintenance trial: 461	At week 6, 14.5% of the Vedolizumab group and 6.8% of the placebo group were in clinical remission (P=0.02); 31.4% and 25.7% of the patients, respectively, had a CDAI-100 response (P=0.23).	Vedolizumab was associated with a higher rate of serious adverse events (24.4% vs. 15.3%), infections (44.1% vs. 40.2%),

					week 52		At week 52, among patients who had a response to induction therapy, 39.0% and 36.4% of those assigned to vedolizumab every 8 weeks and every 4 weeks, respectively, were in clinical remission, as compared with 21.6% assigned to placebo (P<0.001 and P=0.004 for the two vedolizumab groups, respectively, vs. placebo).	and serious infections (5.5% vs. 3.0%). Nasopharyngitis occurred more frequently, and headache and abdominal pain less frequently, in patients receiving vedolizumab than in patients receiving placebo. Antibodies against vedolizumab developed in 4.0% of the patients.
Sands et al., 2014[16]	Effects of vedolizumab induction therapy for patients with Crohn's disease in whom tumor necrosis factor antagonist treatment failed	Placebo-controlled, phase 3, double-blind trial	Vedolizumab (300 mg, intravenous)	Patients with moderately to severely active CD (CD activity index [CDAI] score, 220-400 points), including patients with previous TNF antagonist failure (ie, an inadequate response to, loss of response to, or intolerance of ≥1 TNF antagonists)	Proportion of patients in clinical remission (CDAI, ≤150 points) at week 6 and week 10, and CDAI-100 response (≥100-point decrease in CDAI score from baseline) at week 6	Overall population: 416 (TNF antagonist naive: 101, TNF antagonist failure: 315)	Among patients with previous TNF antagonist failure, 15.2% of those given vedolizumab and 12.1% of those given placebo were in remission at week 6 (P = .433). At week 10, a higher proportion of this population given vedolizumab was in remission (26.6%) than those given placebo (12.1%) (nominal P = .001; relative risk, 2.2; 95% confidence interval, 1.3-3.6). A higher proportion of patients with previous TNF antagonist failure given vedolizumab also had a CDAI-100 response at week 6 than those given placebo (39.2% vs 22.3%; nominal P = .001; relative risk, 1.8; 95% confidence interval, 1.2-2.5).	Adverse event results were similar among all groups.
Vermeire	Efficacy and	Randomised,	Vedolizumab	Adults with	Clinical remission at	410	At Week 52, 48.0% of patients	Injection site

et al., 2022[17]	Safety of Subcutaneous Vedolizumab in Patients With Moderately to Severely Active Crohn's Disease: Results From the VISIBLE 2 Randomised Trial	double-blind, placebo-controlled, phase 3 trial	108 mg SC	moderately to severely active CD who were Week 6 clinical responders (≥70-point decrease in CD Activity Index [CDAI] score from baseline) after vedolizumab 300 mg intravenous induction therapy	Week 52 [primary endpoint; CDAI ≤150], enhanced clinical response [≥100-point decrease in CDAI from baseline], corticosteroid-free clinical remission among patients using a corticosteroid at baseline, clinical remission in anti-tumour necrosis factor [anti-TNF]-naïve patients	(Vedolizumab SC: 275, Placebo: 135)	receiving vedolizumab SC versus 34.3% receiving placebo were in clinical remission [p = 0.008]. Enhanced clinical response at Week 52 was achieved by 52.0% versus 44.8% of patients receiving vedolizumab SC versus placebo, respectively [p = 0.167]. At Week 52, 45.3% and 18.2% of patients receiving vedolizumab SC and placebo, respectively, were in corticosteroid-free clinical remission, and 48.6% of anti-TNF-naïve patients receiving vedolizumab SC and 42.9% receiving placebo were in clinical remission.	reaction was the only new safety finding observed for vedolizumab SC [2.9%].

Abbreviations: CD: Crohn's disease; GEMINI: Gastrointestinal Efficacy of Vedolizumab in Inflammatory Bowel Disease Trials; CDAI: Crohn's Disease Activity Index; MLN0002: Investigational drug code; SC: Subcutaneous; TNF: Tumor Necrosis Factor; VISIBLE: Vedolizumab for Injectable Suspension: Investigating Efficacy in Ulcerative Colitis Studies Assessing Safety and Efficacy for Long-term Maintenance; IV: Intravenous.

Banerjee et al., 2021 reported in a Phase 3, Randomized, Placebo-Controlled Trial that during the induction phase, 14.7% of vedolizumab-treated patients in Asian countries achieved clinical remission at week 6 vs none with placebo.[13] During maintenance, remission rates at 52 weeks with vedolizumab every 4 weeks, every 8 weeks, and placebo were 41.7%, 36.4%, and 0% respectively. Enhanced clinical response rates were 41.7%, 63.6%, and 42.9% respectively. Vedolizumab was generally well-tolerated with 39.7% of patients experiencing an adverse event during induction, compared to 58.8% of patients with placebo.

Feagan et al., 2008 conducted a Randomized, double-blind, controlled trial with MLN0002, a monoclonal antibody targeting the alpha4beta7 integrin (14). Clinical response rates at day 57 were 53%, 49%, and 41% in the MLN0002 2.0 mg/kg, MLN0002 0.5 mg/kg, and placebo groups. Clinical remission rates at day 57 were 37%, 30%, and 21%, respectively (P = .04 for the 2.0 mg/kg vs placebo comparison). 12% and 34% of patients in the 2.0- and 0.5-mg/kg groups had clinically significant human anti-human antibody levels. The most common serious adverse event was worsening of Crohn's disease.

In an integrated study with separate induction and maintenance trials, Sandborn et al., 2013 found that at week 6, 14.5% of the Vedolizumab group and 6.8% of the placebo group were in clinical remission (P=0.02); 31.4% and 25.7% of the patients, respectively, had a CDAI-100 response (P=0.23).[15] At week 52, among patients who had a response to induction therapy, 39.0% and 36.4% of those assigned to vedolizumab every 8 weeks and every 4 weeks, respectively, were in clinical remission, as compared with 21.6% assigned to placebo (P<0.001 and P=0.004 for the two vedolizumab groups, respectively, vs. placebo). Vedolizumab was associated with a higher rate of serious adverse events (24.4% vs. 15.3%), infections (44.1% vs. 40.2%), and serious infections (5.5% vs. 3.0%).

In a Placebo-controlled, phase 3, double-blind trial, Sands et al., 2014 found that among patients with previous TNF antagonist failure, 15.2% of those given vedolizumab and 12.1% of those given placebo were in remission at week 6 (P = .433).[16] At week 10, a higher proportion of this population given vedolizumab was in remission (26.6%) than those given placebo (12.1%) (nominal P = .001; relative risk, 2.2; 95% confidence interval, 1.3-3.6). A higher proportion of patients with previous TNF antagonist failure given vedolizumab also had a CDAI-100 response at week 6 than those given placebo (39.2% vs 22.3%; nominal P = .001; relative risk, 1.8 ; 95% confidence interval, 1.2-2.5). This data suggests that vedolizumab may provide beneficial effects for patients who have previously experienced treatment failure with TNF antagonists, demonstrating higher rates of remission and CDAI-100 response at week 6 and week 10.

Vermeire et al., 2022, in a randomized, double-blind, placebo-controlled, phase 3 trial, focused on the efficacy and safety of subcutaneous Vedolizumab in adults with moderately to severely active Crohn's Disease.[17] Patients included in this study were week 6 clinical responders after vedolizumab 300 mg intravenous induction therapy. At week 52, 48.0% of patients receiving vedolizumab SC versus 34.3% receiving placebo were in clinical remission [p = 0.008]. Enhanced clinical response at Week 52 was achieved by 52.0% versus 44.8% of patients receiving vedolizumab SC versus placebo, respectively [p = 0.167]. Additionally, at Week 52, 45.3% and 18.2% of patients receiving vedolizumab SC and placebo, respectively, were in corticosteroid-free clinical remission. Notably, 48.6% of anti-TNF-naïve patients receiving vedolizumab SC and 42.9% receiving placebo were in clinical remission.

DISCUSSION

This systematic review aimed to critically evaluate and compare the efficacy and safety of Anti-TNF agents (Infliximab, Adalimumab) and Vedolizumab in adult patients diagnosed with CD. Our study's findings indicate the potential efficacy of vedolizumab, particularly as a subcutaneous medication, in promoting clinical remission in Crohn's disease, both among those with previous TNF antagonist failure and those naïve to anti-TNF treatment. This points towards the possibility of vedolizumab being a promising treatment option for patients with moderately to severely active Crohn's Disease, although further studies are needed to fully understand the long-term efficacy and safety profile of this therapeutic agent.

The findings from the included studies collectively suggest that both Anti-TNF agents and Vedolizumab have demonstrated efficacy in the treatment of CD. Anti-TNF agents, such as Infliximab and Adalimumab, target tumor necrosis factor-alpha (TNF-α), a key inflammatory cytokine implicated in the pathogenesis of CD. These agents have shown effectiveness in inducing and maintaining remission, with studies reporting significant clinical response rates and improved quality of life.[18,19] However, it is important to note that a proportion of patients may not respond to or lose response over time with Anti-TNF therapy, emphasizing the need for alternative treatment options.

Vedolizumab, an integrin receptor antagonist, offers an alternative approach by selectively inhibiting leukocyte adhesion and migration into the gut, thereby reducing inflammation.[4] Studies have demonstrated that Vedolizumab is effective in inducing and maintaining clinical remission in CD patients, even in those who have failed previous Anti-TNF therapy.[5,6] It has shown comparable or superior remission rates compared to placebo, with a favorable safety profile. These findings highlight Vedolizumab as a valuable treatment option, particularly for patients who do not respond to or cannot tolerate Anti-TNF agents.

The choice of biologic agent for CD treatment should be guided by several factors, including treatment response, durability of response, safety profile, and individual patient characteristics. The decision to use Anti-TNF agents or Vedolizumab should be individualized, taking into account patient preferences, disease characteristics, and potential risks and benefits. Therapeutic drug monitoring (TDM) can also play a crucial role in optimizing treatment outcomes. TDM helps guide dose adjustments, ensuring adequate drug levels and minimizing the risk of immunogenicity and loss of response.[7]

The comparative effectiveness of Anti-TNF agents and Vedolizumab in CD management remains a subject of ongoing research and debate. While some studies have shown similar efficacy between these agents, others have suggested potential differences in clinical remission rates, response rates, and adverse events.[20] Individual patient factors, such as disease phenotype, severity, previous treatment history, and concomitant medications, may influence treatment response and should be considered in clinical decision-making. It is important to highlight that the efficacy and safety of biologic agents in CD treatment should be balanced with their potential risks. Adverse events, including infections, infusion reactions, and immunogenicity, can occur with both Anti-TNF agents and Vedolizumab.[21] Close monitoring and proactive management of these risks are crucial to ensure optimal outcomes and patient safety.

Limitations of this systematic review include variations in study designs, patient populations, and outcome measures across the included studies. Heterogeneity in patient characteristics, disease severity, and treatment regimens may introduce potential biases and limit the generalizability of the findings. Additionally, the review focused on randomized controlled trials and non-randomized clinical trials, excluding other study designs that may provide valuable insights.

CONCLUSION

The introduction of biologic agents has revolutionized the treatment landscape for CD. Both Anti-TNF agents and Vedolizumab have shown efficacy in inducing and maintaining remission in CD patients. However, the choice of biologic agent should be personalized, taking into account various factors such as treatment response, durability of response, safety profile, and patient preferences. TDM and proactive management of adverse events play crucial roles in optimizing treatment outcomes. TDM allows for individualized dosing and adjustment of biologic agents, ensuring that patients receive the optimal therapeutic benefit. Additionally, proactive management of potential side effects is essential to minimize risks and maximize treatment adherence.

Further research is warranted to explore the comparative effectiveness and long-term outcomes of different biologic agents in CD management. Comparative studies and real-world evidence can provide valuable insights into the relative benefits and risks of Anti-TNF agents and Vedolizumab. Additionally, investigations into the potential role of combination therapies, such as the use of multiple biologic agents or the combination of biologic agents with other treatment modalities, may further enhance treatment outcomes.

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