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Comparison of the Safety and Efficacy of Ustekinumab and Vedolizumab in Patients with Crohn's Disease: A Systematic Review and Meta-Analysis of Propensity Score Matched Cohort Studies

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 November 2024 and was last updated on a 9 November 2024.

INTRODUCTION

Review question / Objective The review question or objective of the document is to compare the safety and efficacy of Ustekinumab and Vedolizumab in patients with Crohn's Disease. The study focuses on evaluating these two drugs through a systematic review and meta-analysis of propensity score-matched cohort studies, aiming to assess clinical outcomes like steroid-free remission, drug discontinuation rates, adverse events, infection rates, and hospitalization during the first year of treatment.

Condition being studied The condition being studied is Crohn's Disease, a chronic inflammatory bowel disease characterized by inflammation of the gastrointestinal tract, leading to symptoms like abdominal pain, diarrhea, fatigue, and weight loss. This study specifically examines the safety and efficacy of Ustekinumab and Vedolizumab as treatment options for patients with Crohn's Disease who have previously experienced failure with anti-TNF therapy.

METHODS

Participant or population The patient population in this study consists of individuals with moderate-to-severe Crohn's Disease who have previously experienced failure with anti-TNF (tumor necrosis factor) therapies. The participants included in the systematic review and meta-analysis were from propensity score-matched cohort studies, aiming to control for confounding factors in the comparative evaluation of Ustekinumab and Vedolizumab treatments.

Intervention The intervention in this study involves the use of two biological drugs, Ustekinumab and Vedolizumab, as treatments for patients with moderate-to-severe Crohn's Disease.

Comparator The comparator in this study is the direct comparison between the two biological drugs, Ustekinumab and Vedolizumab, in treating patients with Crohn's Disease.

Study designs to be included The study includes propensity score-matched cohort studies that provide comparative data on the safety and efficacy of Ustekinumab and Vedolizumab in patients with Crohn's Disease. Only studies that used propensity score matching to reduce confounding biases were included in this systematic review and meta-analysis.

Eligibility criteria Study Population: Patients with moderate-to-severe Crohn's Disease who have previously failed anti-TNF therapy.
Interventions: Comparative studies involving Ustekinumab and Vedolizumab.
Methodology: Studies that applied propensity score matching to control for confounding variables.
Outcomes Reported: Studies must provide data on outcomes such as steroid-free clinical remission, drug discontinuation rates, adverse events, infection rates, and hospitalization within the first year of treatment.
Study Design: Retrospective or observational cohort studies with propensity score matching.
Language: Full-text articles in languages that could be translated, with non-English articles translated as necessary for the analysis.

Information sources Databases: PubMed and Ovid databases were searched for relevant studies
Search Terms: Keywords used in the search included “propensity score,” “ustekinumab,” and “vedolizumab.”

Main outcome(s) Clinical Steroid-Free Remission: Evaluated at 12 ± 4 weeks, 24 ± 4 weeks, and 52 ± 4 weeks after treatment initiation.
Drug Discontinuation Rate: The rate at which patients stopped using Ustekinumab or Vedolizumab within the first year of treatment.
Adverse Events: The occurrence of any adverse effects related to the treatment.
Serious Infections: Infections requiring hospitalization within the first year of treatment.
Hospitalization Rate: The need for hospitalization during the first year of treatment.

Quality assessment / Risk of bias analysis The quality assessment and risk of bias analysis in this study were conducted using the ROBINS-I tool (Risk of Bias in Non-randomized Studies – of Interventions).

Strategy of data synthesis The strategy for data synthesis in this systematic review and meta-analysis involved several key steps. First, data from individual studies were pooled for meta-analysis using statistical software tools, specifically RevMan 5.4.1 and ProMeta 3. Continuous outcomes were summarized using means and standard deviations (SD); for outcomes originally reported in medians and interquartile ranges (IQR) or confidence intervals, mean and SD values were estimated according to established methods. For categorical outcomes, such as remission rates and adverse events, odds ratios (OR) were calculated to facilitate comparison.

The choice of statistical model depended on the level of heterogeneity observed among studies. A random-effects model was applied in cases of high heterogeneity ($I^2 > 50\%$), while a fixed-effect model was used when heterogeneity was low. To assess the degree of heterogeneity, the I^2 statistic was employed, providing a quantitative measure of variability across studies.

Publication bias was evaluated using Egger’s regression asymmetry test and Begg’s test. If publication bias was detected, the “trim and fill” method was used to adjust the results accordingly, thereby ensuring a more accurate synthesis of the evidence. This systematic approach enabled a comprehensive synthesis of the data, managing heterogeneity and minimizing the influence of potential biases.

Subgroup analysis Duration of Clinical Remission: Outcomes were evaluated separately at different time points, namely at 12 ± 4 weeks, 24 ± 4 weeks, and 52 ± 4 weeks, to assess short-term and long-term remission rates.

Sensitivity analysis The "trim and fill" method was employed in this systematic review and meta-analysis to address potential publication bias. This method helps to adjust for bias by estimating the impact of missing studies that may have gone unpublished due to non-significant or unfavorable results. Initially, publication bias was assessed using Begg’s and Egger’s tests, and funnel plots were reviewed to visually inspect asymmetry, which can indicate bias. When significant bias was detected, the trim and fill technique was applied. This process involves "trimming" asymmetrical studies from the funnel plot and then "filling" in the hypothetical missing studies to create a more symmetrical distribution.

Language restriction Only english studies.

Country(ies) involved Italy.

Keywords Crohn’s Disease, Meta-analysis, Biologics, Ustekinumab, Vedolizumab, Comparison.

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