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None declared.

Vedolizumab subcutaneous formulation in maintenance therapy for IBD patients: a systematic review

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Review question / Objective: **(1) P: patients diagnosed with IBD or IBD treated with VDZ at the direction of their physician; (2) I: intervention: VDZ SC; (3) C: if a control group existed in the study, the intervention was VDZ IV and/or PBO; and (4) O: the outcome of the included studies was in line with the review value. Includes: efficacy (clinical remission,endoscopic remission,biochemical remission.); safety/tolerability (AEs, SAEs.);pharmacokinetics(seurm vedolizumab concentrations) and Immunogenicity (anti-vedolizumab antibody (AVA)); (5) S: RCT, non-RCT, observational cohort studies, retrospective study, case series, review, meta-analysis, etc. Repeated reports, animal experiments, clinical studies in non-VDZ SC treatment groups, and related reports unrelated to clinical practice were excluded. The above standards were jointly formulated by the two researchers and implemented independently. If there was a disagreement, a third researcher participated in the decision-making.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 December 2022 and was last updated on 30 December 2022 (registration number INPLASY2022120115).

INTRODUCTION

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Condition being studied: XThe most frequent biologics and other small molecule drugs targeting IBD include infliximab, etanercept, ustekinumab, and vedolizumab. Unlike other drugs that block key inflammatory cytokines or cell surface molecules, VDZ (vedolizumab), a first- and second-line biologic therapy for IBD, does not induce inhibition of systemic inflammatory channels to modulate intestinal inflammation, but rather achieves intestinal therapeutic effects by inhibiting α4β7 integrins to directly and precisely target signaling pathways such as NF-KB. It has been shown that the use of VDZ can achieve similar efficacy to tumor necrosis factor inhibitors (TNFis) when other drug treatments respond inadequately or fail. Surprisingly, Bressler found that VDZ possesses a higher safety record than other biologic agents.
VDZ is administered primarily by intravenous drip. Patients spend a long time on treatment, usually 3 hours or more. Even more distressing is the fact that IBD patients must make regular visits to hospitals or clinics over a long period of time. Fortunately, Takeda has developed a subcutaneous formulation of VDZ that can be self-administered and self-administered, which appears to have the opportunity to be a potentially excellent option for the treatment of patients with moderate to severe IBD. Through a preliminary pharmacokinetic study, the administration was changed from intravenous drip to subcutaneous injection, and the experimental dose and frequency were adjusted from 300 mg Q8W to 108 mg Q2W to achieve equivalent serum drug concentrations. To date, there have been many clinical efficacy studies and patient willingness surveys on VDZ SC. However, systematic studies integrating clinical data on VDZ SC maintenance therapy in patients with IBD are still lacking. Our aim was to provide a more convenient, effective and safe treatment option for patients with IBD by systematically analyzing all current randomized controlled studies on VDZ SC maintenance therapy for inflammatory bowel disease.

METHODS

Participant or population: Patients diagnosed with IBD or IBD treated with VDZ at the direction of their physician.

Intervention: Intervention: VDZSC

Comparator: If a control group existed in the study, the intervention was VDZ IV and/or PBO.

Study designs to be included: RCT; prospective cohort studies.

Eligibility criteria: The outcome need to be defined separately.The primary efficacy endpoint was clinical remission (defined as a total Mayo score of ≤2 and no individual subscore >1. Also defined as HBI ≤4 or PRO2-CD ≤11 in patients with CD and SCCAI ≤2 or PRO2-UC=0 in patients with UC). Secondary efficacy endpoints included endoscopic improvement and biochemical remission, defined as a Mayo endoscopic subscore ≤1 and fecal calprotectin <250 mg/mL, respectively; and corticosteroid-free remission (defined as discontinuation of oral corticosteroids in patients receiving oral corticosteroids at baseline and subsequent clinical remission at endpoint). Clinical remission at endpoint in patients previously treated with TNF-α antagonists and initial TNF-α antagonist therapy was an exploratory endpoint.The safety assessment includes all adverse events (AEs) and serious AEs. these events may result from changes or exacerbations in the patient's clinical presentation, as well as from blood, urine, etc., or ECG findings. All AEs, regardless of their causality, should be

included.Pharmacokinetic and immunogenicity endpoints were derived from the results reported in the included studies. Ignoring inconsistencies in assays across studies, Positive AVA status was defined as ≥ 1 positive AVA result from predose to endpoint.

Information sources: Embase, PubMed, the Web of Science, the Cochrane four databases and ClinicalTrials.gov .

Main outcome(s): The primary efficacy endpoint was clinical remission.Secondary efficacy endpoints included endoscopic improvement and biochemical remission; and corticosteroid-free remission . Clinical remission at endpoint in patients previously treated with TNF-α antagonists and initial TNF-α antagonist therapy was an exploratory endpoint.The safety assessment includes all adverse events (AEs) and serious AEs.Pharmacokinetic and immunogenicity endpoints were derived from the results reported in the included studies.

Quality assessment / Risk of bias analysis: The CochranQ test was calculated, and the resulting I2 statistic was used to assess study heterogeneity to determine whether the analysis used a random-effects model or a fixed-effects model. Fixed-effects models were used when heterogeneity was absent or present but small, and random-effects models were used when it was large; if heterogeneity was great, meta-analysis was discarded and only systematic evaluation was performed. P values below 0.05 will be considered statistically significant. Funnel plots were used to assess publication bias when a sufficient number of studies were included.

Strategy of data synthesis: Data from included studies were statistically analyzed using Cochran software Review Manager 5.4 (software from the Cochrane Collaboration (London, United Kingdom)).OR (95% CI) indicates dichotomous variables included in the study for all target outcomes and 95% CIs were combined using the Mantel-Haenszel method.

Subgroup analysis: UC and CD patients were divided into two subgroups for analysis.

Sensitivity analysis: The stability of the combined results of the fixed-effects model was assessed by means of a random-effects model.

Country(ies) involved: China.

Keywords: Vedolizumab subcutaneous, IBD, efficacy, adverse reactions, systematic evaluation, serum VDZ concentration, maintenance therapy.

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