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Clinical Insights into IL-23 Inhibition: Risankizumab for Crohn's Disease Through a Systematic Review and Meta-Analysis of Randomized Controlled Trials

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ADMINISTRATIVE INFORMATION

Support - N/A.

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 4 March 2025 and was last updated on 4 March 2025.

INTRODUCTION

Review question / Objective To investigate the treatment effect of Risankizumab for Crohn's Disease.

Rationale Crohn's disease is a chronic inflammatory disorder with rising global prevalence, marked by abdominal pain, diarrhea, and fatigue. Interleukin (IL)-23 plays a pivotal role in Crohn's disease pathogenesis, making it a therapeutic target. Risankizumab, a monoclonal antibody targeting the IL-23 p19 subunit, has shown potential in clinical trials. Therefore, we would like to perform a systematic review and meta-analysis to investigate the treatment of Risankizumab for Crohn's Disease.

Condition being studied The PICO (population, intervention, comparison, outcome) setting of the current meta-analysis included: P (Population): Participants with Crohn's disease. I (Intervention): Risankizumab treatment. C (Comparison): Placebo or standard treatment (e.g., TNF inhibitors, corticosteroids). O (Outcome): Changes in disease activity (e.g., Crohn's Disease Activity Index [CDAI]), endoscopic remission or adverse events.

METHODS

Search strategy Two authors (P.-F.H. and C.-F.C.) made independent electronic searches in the PubMed, Embase, Cochrane CENTRAL, Web of Science and ClinicalTrials.gov with keyword of ("Risankizumab") AND ("Crohn's Disease" OR "Inflammatory Bowel Disease" OR "IBD") AND ("efficacy" OR "treatment outcome" OR "clinical trial") AND ("safety" OR "adverse effects" OR "side effects") AND ("quality of life" OR "QOL") AND ("endoscopic remission" OR "mucosal healing") AND ("biologics" OR "Interleukin-23 inhibitor").

Participant or population Human participants.

Intervention Risankizumab treatment.

Comparator Placebo.

Study designs to be included Randomized controlled trials.

Eligibility criteria To generate a recruited study list, the following inclusion criteria will be used: (1) RCTs involving human participants, (2) RCTs with quantitative assessments of outcome before and after Risankizumab, and (3) trials providing data on pre- and post-intervention changes in disease activity.

Information sources Two authors (P.-F.H. and C.-F.C.) made independent electronic searches in the PubMed, Embase, Cochrane CENTRAL, Web of Science and ClinicalTrials.gov with keyword of ("Risankizumab") AND ("Crohn's Disease" OR "Inflammatory Bowel Disease" OR "IBD") AND ("efficacy" OR "treatment outcome" OR "clinical trial") AND ("safety" OR "adverse effects" OR "side effects") AND ("quality of life" OR "QOL") AND ("endoscopic remission" OR "mucosal healing") AND ("biologics" OR "Interleukin-23 inhibitor").

Main outcome(s) This study primarily assessed changes in clinical remission, clinical response, and endoscopic remission following treatment with Risankizumab or placebo. The validity and appropriateness of the scales used in each trial were also examined by checking the pertinent references. If there were more than one scoring system for fatigue evaluation in a single trial, the index test included for meta-analysis was decided by the consensus of two authors (P.-F.H. and C.-F.C.)

Additional outcome(s) The secondary outcome was treatment-related adverse event rates. The aforementioned outcomes were quantified by odds ratios.

Data management Two independent authors (P.-F.H. and C.-F.C.) extracted data from the recruited studies, encompassing demographic data, study design, details of Risankizumab and placebo regimens, and values of the primary and secondary outcomes. The evaluators paid special attention to the effect direction of the scale used in each trial to avoid mis-interpretation. In situations where the data was unavailable in the published articles, we contacted the corresponding authors to obtain the originaldata.

Quality assessment / Risk of bias analysis To investigate the methodological quality of recruited studies, we used the Cochrane risk-of-bias tool for randomized trials, version 2 (RoB 2), which consisted of 6 main items: randomization process, intervention adherence, missing outcome data, outcome measurement, selective reporting, and overall risk of bias. In the intervention adherence section of RoB 2, there are two options for literature assessment: intention-to-treat (intervention assignment) or per-protocol (intervention adherence). In this meta-analysis, we chose the per-protocol evaluation, since it fits the design of our included studies.

Strategy of data synthesis Because of the heterogeneity of the target populations in the enrolled studies, the current meta-analysis was conducted with a random-effects model, using Comprehensive Meta-Analysis software, version 3 (Biostat, Englewood, NJ). A two-tailed p value less than 0.05 was considered statistically significant. We chose Hedges' g and 95% confidence intervals (CIs) to quantify the primary outcomes (changes in fatigue scores). A Hedges' g of 0.2, 0.5, and 0.8 is considered a small, moderate, and large effect size, respectively. We chose odds ratios and their 95% CIs to investigate the secondary outcome (treatment-related adverse event rates).
The I2 and Cochran's Q statistics were used to evaluate the degree of heterogeneity among studies. An I2 value of 25%, 50%, and 75% was considered low, moderate, and high heterogeneity, respectively.

Subgroup analysis Meta-regressions of the treatment effects on Risankizumab doses and treatment durations were conducted to see if the relieving effect of Risankizumab correlated with the aforementioned parameters.

Sensitivity analysis To confirm the robustness of the meta-analysis, the sensitivity analyses were performed using one-study removal method to see if there was a significant change in the summary effect size after removing a particular trial from the analysis.

Language restriction No language limit.

Country(ies) involved Taiwan.

Keywords Crohn's disease; Risankizumab; IL-23 inhibitors; Meta-analysis; Clinical remission; Endoscopic remission.

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