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Compare the efficacy and safety of fecal microbiota transplantation (FMT) with biologic agents and small molecule drugs for the treatment of moderate to severe ulcerative colitis (UC)：A protocol of systematic review and network meta-analysis

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ADMINISTRATIVE INFORMATION

Support - National Science and Technology Council (112-2320-B-182-036-MY3 and 112-2320-B-182-042-MY3).

Review Stage at time of this submission - Data analysis.

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 13 December 2024 and was last updated on 13 December 2024.

INTRODUCTION

Review question / Objective This systematic review and network meta-analysis (NMA) aim to compare the relative efficacy and safety of biologics, SMDs, and FMT in patients with moderate-to-severe UC.

Condition being studied Ulcerative colitis (UC) is a chronic and idiopathic condition that can be debilitating. It is clinically characterized by symptoms such as bloody diarrhea, abdominal pain, and tenesmus. The gut microbiome of UC patients differs significantly from that of healthy individuals. Studies have found that patients with UC, whether in active or remission phases, tend to have higher levels of Clostridia and adherence-invasive strains of Escherichia coli compared to healthy individuals. These alterations in the gut microbiota may both result from and contribute to chronic inflammation in the intestinal mucosa. The unique composition of the microbiota along different segments of the gastrointestinal tract could lead to localized inflammation associated with distinct microbial communities in UC . UC arises from immune system deficiencies within the gastrointestinal tract, and a definitive cure remains unavailable. Dysbiosis of the gut microbiota disrupts immune function, promoting inflammation and potentially initiating UC. Additionally, individuals with a genetic predisposition to UC may exhibit microbiome changes even before clinical symptoms develop.

METHODS

Participant or population Adult patients with moderate-to-severe UC (defined as a Mayo score of 6-12 and an endoscopic subscore of 2-3).

Intervention Approved biologics (infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, etrolizumab) or SMDs (tofacitinib, upadacitinib, filgotinib, ozanimod, etrasimod, TD-1473) or FMT.

Comparator Placebo or an active comparator.

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria Eligible studies met the following criteria:
1.Randomized controlled trials (RCTs) involving adult patients with moderate-to-severe UC (defined as a Mayo score of 6-12 and an endoscopic subscore of 2-3).
2.Patients included could be biologic-naïve or previously treated with at least one biologic agent.
3.Studies comparing approved biologics (infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, etrolizumab) or SMDs (tofacitinib, upadacitinib, filgotinib, ozanimod, etrasimod, TD-1473) or FMT against placebo or an active comparator.
4.Studies reporting clinical remission (Mayo score ≤ 2 with no subscore > 1) and endoscopic improvement (Mayo endoscopic subscore of 0 or 1).

Information sources PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL).

Main outcome(s) Relative treatment rankings for clinical remission, endoscopic improvement, adverse events (AEs), and serious adverse events (SAEs) were calculated using the surface under the cumulative ranking (SUCRA).

Quality assessment / Risk of bias analysis RoB2 tool (a revised Cochrane risk-of-bias tool for randomized trials).

Strategy of data synthesis We conducted a network meta-analysis using a multivariate frequentist approach with STATA software (version 18). Relative treatment rankings for clinical remission, endoscopic improvement, adverse events (AEs), and serious adverse events (SAEs) were calculated using the surface under the cumulative ranking (SUCRA). A higher SUCRA score indicates better efficacy, while a lower SUCRA score reflects improved safety outcomes (fewer adverse events).

Subgroup analysis Exploratory analyses evaluated clinical remission and endoscopic improvement for induction and maintenance therapies in biologic-naïve and biologic-experienced populations. These analyses incorporated studies that included data stratified by prior biologic exposure.

Sensitivity analysis No sensitivity analysis will be applied.

Language restriction No language limited will be applied.

Country(ies) involved Taiwan.

Keywords Fecal microbiota transplantation, Ulcerative colitis; biologic agents; small molecular drugs; Network meta-analysis.

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