NON-INTERVENTIONAL/LOW-INTERVENTIONAL STUDY TYPE 1 STUDY REPORT ABSTRACT

Title: A network meta-analysis of real-world studies comparing tofacitinib with other advanced therapies in the treatment of moderate-to-severe ulcerative colitis

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Keywords: network meta-analysis, observational study, real-world data, tofacitinib, ulcerative colitis

Rationale and background: Ulcerative colitis (UC) is a chronic idiopathic inflammatory bowel disease of the colon that causes continuous mucosal inflammation starting in the rectum and extending to the more proximal colon, with variable extents. Tofacitinib (Xeljanz®) is an oral JAK inhibitor for the treatment of moderate-to-severely active UC. A meta-analysis of real-world studies demonstrated the effectiveness of tofacitinib in a highly refractory population of patients with moderate-to-severe UC. Tofacitinib was also shown to have an acceptable safety profile.

Several network meta-analyses (NMA) have been published comparing efficacy and safety of biologics and small molecules for the treatment of moderate-to-severe UC. However, all these NMAs were conducted using data from the randomized trials. Despite the compelling evidence on efficacy and safety of tofacitinib from clinical and real-world studies, there is lack of evidence about the comparative effectiveness and safety of tofacitinib with other therapies approved for the treatment of moderate-to-severely active UC from real-world studies.

The purpose of the study is to assess the feasibility and conduct a NMA to compare the real-world effectiveness and safety of tofacitinib with other advanced therapies in the treatment of moderate-to-severe UC.

Research question and objectives:

Research questions to be addressed by this study are as follows:

1. What is the real-world effectiveness of tofacitinib, compared to alternative advanced therapies, for the treatment of moderate-to-severe UC?

2. How does the safety profile of tofacitinib compare to these alternative advanced therapies?

The primary objectives for this study are:

1. To estimate the difference in the likelihood of achieving a clinically meaningful response, in terms of effectiveness outcomes, between patients treated with tofacitinib compared to other advanced therapies.
2. To estimate the relative risk of serious adverse events (AEs) between patients treated with tofacitinib versus other advanced therapies.

The secondary objectives for this study are:

1. To estimate the incidence rate (IR) of various AEs, and of mortality, on each therapy.

Study design: Analyses will be performed on data collected from studies published in literature in the form of a systematic literature review (SLR) and no patient enrollment will be done. The SLR was conducted to identify the real-world studies reporting effectiveness and/or safety outcomes of advanced therapies for moderate-to-severe UC.

Setting: A comprehensive literature search was performed using the Embase® and MEDLINE® databases through the Embase.com platform from 01 January 2005 to 30 April 2023.

Subjects and study size, including dropouts: Not applicable.

Variables and data sources: Prospective and retrospective observational studies were included. NMAs were conducted based on comparative studies only using a random effects model if the evidence formed a connected network. Additional NMAs were conducted based on both comparative and single-arm studies to incorporate all available information. Single-arm studies of different advanced treatments were matched based on similarity in baseline characteristics.

Results: Ninety-five studies were included in NMAs evidence synthesis (68% studies had mixed population and 11% had biologic-exposed patients). In the induction phase, tofacitinib and infliximab were shown to have highest probability of being the most effective treatments for clinical response; infliximab was also ranked first for clinical remission. In the maintenance phase, infliximab was ranked first for clinical response; ustekinumab was ranked first for clinical remission.

Discussion: The observations from this NMA based on real-world data studies are consistent with findings from NMA based on RCTs. The findings from this NMA, taken together with evidence from RCTs NMA, will support clinicians in decision-making in selecting the most appropriate therapy for treatment of patients with moderate-to-severe UC in clinical practice.

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