



Can Anti-Tumor Necrosis Factor Agents Be Discontinued in Patients with Inflammatory Bowel Disease?

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See “Long-term Outcomes after the Discontinuation of Anti-Tumor Necrosis Factor- α Therapy in Patients with Inflammatory Bowel Disease under Clinical Remission: A Korean Association for the Study of Intestinal Disease Multicenter Study” by Joo Hye Song, et al. on page 752, Vol. 15, No. 5, 2021

Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's colitis (CD), are characterized by chronic and recurrent inflammation of the gastrointestinal tract. Anti-tumor necrosis factor (TNF) agents proved to be effective and safe in IBD.^{1,2} However, there are still concerns about the risk of malignancy and infections after long-term use of anti-TNF agents.^{3,4} There have been few data regarding the discontinuation of anti-TNF agents in IBD patients who achieved remission. This paper presents a study that focuses on the discontinuation of anti-TNF agents and evaluates risk factors in predicting relapse of the disease.

In the current issue, Song *et al.*⁵ conducted a retrospective, multicenter, uncontrolled study. They analyzed a total of 109 IBD patients (71 CD and 38 UC) treated with a first line anti-TNF agent (93 infliximab, 15 adalimumab, or one golimumab), and the median duration of the anti-TNF agent treatment was 12 months (range, 9.0 to 26.5 months). The cumulative relapse rates at 1, 2, 3, and 5 years for IBD patients were 17.4%, 32.9%, 46.7%, and 62.9%, respectively. The cumulative relapse rates for CD patients were 11.3%, 31.4%, 46.7%, and 62.5%, and those for UC patients, were 28.9%, 34.8%, 45.3%, and 60.9%, respectively.⁵ They suggested discontinuation owing to patients' preference (vs clinician's decision) and adalimumab group (vs infliximab group) as risk factors of disease relapse in CD patients. The non-mucosal healing group (vs mucosal healing group) in UC was suggested to be a high-risk group of disease relapse. Despite its retrospective design, lack of therapeutic

drug monitoring, and inadequate measurement of endoscopic parameters, this study appears to be meaningful because it is the first report about the discontinuation of anti-TNF agents in the real-life clinical practice in Korea.

Recently, Kobayashi *et al.*⁶ performed a first multicenter, open-labeled randomized controlled trial (RCT) in patients with UC treated with first line infliximab, and the median duration of infliximab treatment in discontinued infliximab group was 164.6 weeks. The median disease duration of discontinued infliximab group was 5.4 years. The cumulative relapse rates at 8, 16, 24, 32, 40, and 48 weeks for UC patients were 6.5%, 23.9%, 26.1%, 32.6%, 34.8%, and 45.7%, respectively. The relapse rates of UC in the study by Song *et al.* was relatively lower, approximately 20%, compared to this RCT. The study population of in the study by Song *et al.* had a higher rate of ulcerative proctitis compared to the study by Kobayashi *et al.* (23.7% vs 2.0%). Also, the maintenance duration of anti-TNF in the study by Song *et al.* was relatively shorter compared to the study by Kobayashi *et al.* (48 weeks vs 164.6 weeks). The reasons for discontinuation of anti-TNF agents were various in real-life settings, which includes not only clinician's decision but also patient's preference. The relatively shorter maintenance duration of anti-TNF may indicate a lower inflammatory disease burden, which might have affected the outcomes.

In terms of CD, Louis *et al.*⁷ performed a prospective, multicenter, uncontrolled trial with 125 patients treated with first line infliximab, and the median duration of inf-



liximab treatment was 2.2 years. The median disease duration of discontinued infliximab group was 7.8 years. The cumulative relapse rates at 1 and 2 years were 43.9% and 52.2%, respectively, which was also higher compared to the study by Song *et al.* The study population in the study by Song *et al.* had a lower rate of current smoking compared to the study by Louis *et al.* (7.0% vs 39.0%), which could affect the different relapse rates between the two studies. However, the baseline characteristics in the study by Song *et al.* was not better compared to the study by Louis *et al.* in terms of higher rates of ileum or ileo-colonic location of disease (70.4% vs 68%), stricturing behavior of disease (22.5% vs 10.0%), perianal disease (35.0% vs 59.2%), and previous history of intestinal surgery (25.4% vs 22.0%). The retrospective real-life study design might have affected the study outcomes and reduced relapse rates.

The re-treatment with the same anti-TNF was effective in 96.1% (50/52 patients) in the study by Song *et al.* The poor response rate to the re-treatment was reported to be 9% (4/46 patients) and 12% (5/43 patients) in the previous RCTs,^{6,7} which could be related to the immunogenicity of the anti-TNF agent.

This study showed long-term outcomes after the discontinuation of anti-TNF agents in Korea. However, careful consideration should be required before deciding the discontinuation of anti-TNFs, because of still its high rates of relapse and possible immunogenicity. Further prospective RCTs should be warranted for the discontinuation issue of anti-TNFs. Also, predicting factors including clinical, biochemical, and molecular parameters should be determined to appropriately select patients who can discontinue the drug without future development of disease relapse.

CONFLICTS OF INTEREST

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