

Safety of Tofacitinib in the COVID-19 Pandemic—Enough Is Not Enough

To the Editors,

We have read with great interest the brief report by Agrawal et al¹ reporting the incidence of fatal outcomes of COVID-19 in 37 patients with inflammatory bowel disease (IBD) treated using tofacitinib compared with all other patients out of 2,326 patients who received at least 1 IBD medication in the SECURE-IBD database through September 2020. The authors concluded that the use of tofacitinib in patients with IBD is not associated with severe COVID-19. The SECURE-IBD database is a valuable international, pediatric, and adult voluntary reporting system to monitor and report on outcomes of COVID-19 occurring in patients with IBD. Until quite recently, the SECURE-IBD database included information on 4,735 patients. Only 72 patients were treated with tofacitinib according to the database in contrast to 1,581 patients treated using an anti-tumor necrosis factor (TNF) therapy without classical immunomodulators. Two of the 72 (3%) patients with IBD treated using tofacitinib and who had COVID-19 suffered a fatal outcome.²

Primary data collection within registries like SECURE-IBD allows an analysis of potential adverse effects and harmful events in a real-world setting. The strengths of registries depend on the number of observed events, and a meaningful

reporting bias should be considered. If the event number is low, misinterpretations are possible; however, if only 2 more patients treated using tofacitinib had suffered a fatal outcome, then anti-TNFs would be considered a significantly better type of treatment. In contrast, the SECURE-IBD registry indicates a low rate of fatal events in the 1,581 patients who were receiving anti-TNFs, which allows the database to derive a high degree of security. Furthermore, the authors combined all “non-tofacitinib” groups together, including patients using systemic steroid therapy. Risk factors for severe COVID-19 include systemic corticosteroid and 5-aminosalicylate use, whereas anti-TNFs have not been associated with severe COVID-19.³ Severe forms of COVID-19 occur as a result of exacerbated inflammation with an excess release of cytokines. Thus, the repurposing of biologics such as anti-TNFs has emerged as a logical strategy to quench inflammation and improve the outcome of patients with COVID-19 as shown in a recent case series.⁴

Given the occasional reports of fatal COVID-19 courses even in children treated with tofacitinib⁵ and the recently announced failure of the non-inferiority criteria of tofacitinib compared to anti-TNFs in regard to major adverse cardiovascular events and malignancies in patients with rheumatoid arthritis (<https://www.pfizer.com/news/press-release/press-release-detail/pfizer-shares-co-primary-endpoint-results-post-marketing>), we suggest a very safety-oriented use of tofacitinib even in patients with IBD during the COVID-19 pandemic and thereafter.

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