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LETTER

Comment on: "Retrospective Claims Analysis Indirectly Comparing Medication Adherence and Persistence Between Intravenous Biologics and Oral Small-Molecule Therapies in Inflammatory Bowel Diseases"

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Key Summary Points

The authors of Moran et al. used mutually exclusive IBD and RA infliximab treatment data to bridge differences across the unique inflammatory diseases, concluding that, after adjustment, adherence was higher with infusions than oral medications.

The analysis by Moran et al. does not take into account a number of important factors:

1. No discussion of reasons for discontinuation of treatment, nor the important differences between RA and IBD patient populations, was included in the manuscript.
2. Previous studies have shown wide variability in the concept of adherence, as well as its measurement, which could affect the conclusions of a study such as that presented by Moran et al.
3. Real-world data comparing tofacitinib with common biologics for the treatment of RA reported persistence and adherence of tofacitinib were at least comparable to that of the biologics.

We believe that there are pitfalls associated with the indirect method applied by Moran et al. and their results should be interpreted with caution.

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Dear Editor,

We read with great interest the article by Moran et al. entitled "Retrospective Claims Analysis Indirectly Comparing Medication Adherence and Persistence Between Intravenous Biologics and Oral Small-Molecule Therapies in Inflammatory Bowel Diseases" [1].

In this retrospective cohort analysis of a claims database of adult patients diagnosed with either inflammatory bowel disease (IBD) or rheumatoid arthritis (RA), the authors investigate adherence and persistence with respect to vedolizumab in IBD, tofacitinib in RA, or

infliximab in RA or IBD treatment. Using mutually exclusive IBD and RA infliximab treatment data to bridge differences across the unique inflammatory diseases, the authors conclude that, after adjustment, adherence was higher with infusions than oral medications [1]. These results are in contrast to findings from previous well-conducted studies [2, 3]. Furthermore, the analysis by Moran et al. does not take into account a number of important factors, and we suggest relies on questionable methodology. These limitations cast doubt on the validity of their findings and overall conclusions, which we believe should be brought to the attention of the authors and your readers.

Although the authors of the paper noted that "there are several reasons for discontinuation that pertain to each disease" as a limitation of the study [1], no discussion of reasons nor the important differences between RA and IBD patient populations was included in the manuscript, such as age of the patients, presence of comorbidities, and number of concomitant therapies. Indirect comparisons utilizing observational studies, such as that described in Moran et al., are uncommon, since the heterogeneity of patient populations in the real world make such comparisons difficult. The study also failed to recognize tofacitinib dosing differences between the two diseases, both in terms of dose strength and overall posology. In accordance with US prescribing information, the recommended tofacitinib dose for RA is 5 mg twice daily (BID) or 11 mg once daily, whereas for ulcerative colitis (UC), the recommended dose is 10 mg BID for induction (8 weeks, continue for a maximum of 16 weeks if needed) followed by 5 mg BID or 10 mg BID for maintenance (use of 10 mg BID beyond induction should be limited and used for the shortest duration) [4]. Furthermore, for tumor necrosis factor inhibitors, including infliximab, real-world data have shown that changes in dose and dose schedules are more common for patients with IBD vs those with RA [5, 6], highlighting the complexity involved in comparing the same therapies across different disease populations. It is also noteworthy that tofacitinib is indicated for UC, in contrast to vedolizumab and infliximab, which have indications for both Crohn's disease and UC, reiterating the inappropriateness of these comparisons, which included patients with UC and also patients with Crohn's disease.

A systematic review of 24 studies of RA, spondyloarthritis, and psoriatic arthritis examined adherence to biologic therapies and concluded that there was wide variability in the concept of adherence as well as in its measurement [7]. The choice of methods used might therefore be expected to affect the conclusions of a study such as that presented in Moran et al. Of note, although two methods were used to evaluate adherence, significant differences between vedolizumab/IBD and tofacitinib/RA were observed only for one of them after the adjustment method was applied [1].

Finally, published data on the concept of persistence and adherence with tofacitinib have demonstrated 2- and 5-year estimated drug survival rates of 75.5% and 49.4%, respectively, in a clinical trial setting [2], while real-world data comparing tofacitinib with common biologics (adalimumab, etanercept, and abatacept) for the treatment of RA reported persistence, and adherence of tofacitinib was at least comparable to that of the biologics [3].

As stated in the article by Moran et al., their results are not generalizable and need to be confirmed in tofacitinib-treated IBD patients. In the absence of direct study in tofacitinib-treated patients with UC, we believe that there are pitfalls associated with the indirect method applied by Moran et al. (as noted by the authors themselves) that amount to an uneven evaluation and comparison with potential for bias, and therefore the results should be interpreted with caution. This should be brought to the attention of your readership and prescribers.

Sincerely,

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Peer Review. Please note, contrary to the journal's standard single-blind peer-review process, as a letter this article underwent review by a member of the journal's Editorial Board.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed for this letter.

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