Editorial: real-world evidence of tofacitinib and vedolizumab in ulcerative colitis-are we one step closer to better positioning therapies after anti-TNF failure? Authors' reply

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INVITED EDITORIAL

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First of all, we would like to thank Drs Ernest-Suarez and Lu for their interest in our real-world comparison between tofacitinib and vedolizumab in patients with ulcerative colitis after failure of anti-TNF therapy.[1,2] Drug sequencing is currently a burning question in inflammatory bowel disease, especially in ulcerative colitis owing to the growing number of available therapeutic classes with different mechanisms of action. Beyond crude efficacy, the impact of the therapeutic sequence, that is whether treatment A followed by treatment B achieves the same efficacy as the reverse sequence, is a major question. The STARTER project has been specifically built to answer this question and will start soon. It is a French multicenter randomised controlled trial comparing four therapeutic sequences in biologic-naïve UC patients. Each sequence will start with a different class of medication, that is anti-TNF agent, anti-integrin, anti-IL12/IL23 or JAK inhibitor.

To compare the efficacy of two drugs after anti-TNF failure, no head-to-head trials are currently available, and network meta-analyses rely on a low number of studies for each drug.[3,4] Thus, real-world indirect comparisons adjusted using propensity scores are of great interest. In our work, the first message apply to vedolizumab. Contrary to what may sometimes be suggested, vedolizumab can lead to remission as soon as week 2 in one third of the patients. However, a longer period is required for some patients up to week 14, meaning that the time to observe response to vedolizumab can range from week 2 to week 14. In addition, we found that vedolizumab is less effective in case of more severe (Mayo score > 6 and CRP > 30) or more refractory (primary failure to at least biologic) UC. The second message concern tofacitinib. Contrary to vedolizumab, we did not find any factor associated with tofacitinib failure. Of note, we reported a very high rate of relapse after decreasing the dose from 10 to 5 mg *b.i.d* in patients achieving remission at week 8 (48%). This result should lead to caution before dose de-escalation in patients treated with tofacitinib. We also observed a delayed response (week 16) in one-quarter of patients receiving tofacitinib without any response at week 8, underlining that tofacitinib therapy should be maintained at least 16 weeks before considering therapeutic failure. Finally, our data suggest that tofacitinib could be more effective than vedolizumab after anti-TNF failure in terms of endoscopic and histological remission. It is in line with the results of a Dutch cohort, showing that tofacitinib-treated patients were more likely to achieve corticosteroid-free clinical remission and biochemical remission at weeks 12, 24 and 52 compared with vedolizumab-treated patients.[5]

However, efficacy is not the only parameter impacting therapeutic decision-making. Except for the question of drug reimbursement by the healthcare system, which is highly different across the countries, the choice of the best therapy should rely on the triptych

TABLE 1 Arguments to choose between tofacitinib and vedolizumab after failure to anti-TNF therapy in patients with UC.

	Favouring tofacitinib	Favouring vedolizumab
Efficacy[2,5]		
Rate of steroid-free clinical remission	✓	
Rate of endoscopic remission	✓	
Rate of histological healing	✓	
Time to efficacy	✓	
Severe UC	✓	
Primary failure to at least one biologic	✓	
Joint extra-intestinal manifestations	✓	
Safety[4,7]		
Risk of cardiovascular events		✓
Risk of thromboembolism events		✓
Risk of lung neoplasm		✓
Age > 65 years-old		✓
Comorbidities		✓
Acceptability[6]	✓	

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efficacy-safety-acceptability.[6] The arguments for favouring tofacitinib or vedolizumab after anti-TNF failure are summarised in Table 1.

AUTHOR CONTRIBUTIONS

Anthony Buisson: Conceptualization (lead); writing – original draft (lead).

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LINKED CONTENT

This article is linked to Buisson et al papers. To view these articles, visit https://doi.org/10.1111/apt.17305 and https://doi.org/10.1111/apt.17351

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