Received: 20 January 2021 | Accepted: 22 January 2021

DOI: 10.1111/apt.16287

AP&T Alimentary Pharmacology & Therapeutics WILEY

Letter: SARS-CoV-2 infection in two inflammatory bowel disease patients treated with dual targeted therapy—Authors' reply

We thank Privitera et al for detailing COVID-19 infection in two of 11 IBD patients receiving dual targeted therapy.[1] Neither patient was hospitalised nor experienced severe disease; however, viral shedding extended beyond 20 days raising concern that dual targeted therapy might increase the risk of prolonging viral illness.

The role of dual targeted therapy has recently expanded with experiential use in medically refractory IBD and in those with active extraintestinal manifestations despite treatment.[2-4] Efficacy appears promising; however, most data are retrospective. Safety profiles are variable depending on treatment combination, and safety and cost concerns remain the prominent deterrent.[2-4] To date, there has been only one published randomised-controlled trial of combination biologic therapy comparing infliximab versus infliximab with an anti-integrin (natalizumab) in persistently active Crohn's disease.[5] There was no difference in safety, with a trend towards clinical improvement in the dual targeted therapy group ($P = 0.084$). Importantly, the study was inadequately powered to assess efficacy and detect rare adverse events.[5]

There are few reports of patients on dual targeted therapy and coexisting COVID-19. There has been one report of a 24-year-old male patient with Crohn's disease on ustekinumab and adalimumab. He asymptomatically tested positive for SARS-CoV-2, and remained asymptomatic at weeks 2 and 6.[6] The SECURE-IBD registry revealed that active disease, corticosteroids, thiopurines and 5-ASAs are associated with poorer outcomes in COVID-19.[7] Biologic monotherapy was not associated with worse outcomes and hence dual targeted therapy as a means of avoiding corticosteroid and immunomodulators presents an enticing option in uncontrolled IBD. The described cases of dual targeted therapy and mild COVID-19 are reassuring. Furthermore, biologic monotherapy is being assessed for treatment of severe COVID-19 given its potential to suppress the aberrant systemic inflammatory response. Dual targeted therapy may hence theoretically confer benefit. However, whether there is increased risk in COVID-19 acquisition or disease severity with dual targeted therapy remains unclear given such few cases. Thus, guidance for recommendations within this population is limited.[8]

Finally, SARS-CoV-2 viral shedding is widely acknowledged with RNA detected in upper respiratory specimens of recovered COVID-19 patients for up to 12 weeks.[9] However, up to 95% of severely or critically ill patients, including immunocompromised, do not have replication-competent virus 15 days post symptom onset and are not considered infectious.[10] Hence, prolonged viral shedding beyond symptom resolution does not imply active disease nor increased infectious period, and thus likely holds minimal clinical relevance. The Centers for Disease Control guidelines for discontinuation of transmission-based precautions for COVID-19 focus on a symptom-based approach.[10]

Ultimately, dual targeted therapy is an exciting and evolving field within IBD. The pandemic is likely to affect our clinical practices for years to come, highlighting the need to minimise long-term corticosteroid exposure through proactive escalation to targeted therapies. Individualising and optimising treatment plans while being cognisant of infectious complication risks remain the fundamental therapeutic goal.

ACKNOWLEDGEMENT

The authors' declarations of personal and financial interests are unchanged from those in the original article.[8]

LINKED CONTENT

This article is linked to Al-Ani et al and Privitera et al papers. To view these articles, visit https://doi.org/10.1111/apt.15779 and https://doi.org/10.1111/apt.16297

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