of endogenous ACE2-Ang 1-7 axis activation. These data suggest that, in addition to the use of angiotensin receptor blockers and/or ACE inhibitors and/or ROCK inhibitors, vitamin D may also be beneficial to increase ACE2 and reduce ROCK activity. Furthermore, a telephone survey of over 100 of our Gitelman's and Bartter's patients, all of whom were from hotspots of the COVID-19 pandemic in Northern Italy, found none of them infected with COVID-19.[10] This is significant evidence (95% CI 0%-3% compared to the estimated true COVID-19 prevalence in Northern Italy of 8.7%, 95% CI 8.7%-8.8%, $P = 0.004$), that increased ACE2 and reduced ROCK activity may have beneficial effects in COVID-19 prevention and/or treatment.

Given the rapidly evolving nature of the COVID-19 pandemic and in consideration of the reported effects of vitamin D on ACE2 and ROCK, vitamin D might also be used to reduce the severity of COVID-19.

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This article is linked to Panarese et al and Kumar et al papers. To view these articles, visit https://doi.org/10.1111/apt.15752 and https://doi.org/10.1111/apt.15801.

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Letter: ciclosporin and vedolizumab for steroid-refractory ulcerative colitis

EDITORS,

We read with interest the recently published article by Ollech et al examining the efficacy and safety of induction therapy with calcineurin inhibitors transitioned to vedolizumab in steroid-refractory ulcerative colitis patients.[1] There is a great need to evaluate possible therapeutic strategies in severe steroid-refractory inflammatory bowel disease that can help to assure colectomy-free survival with acceptable long-term safety profile. Here, we would like to share our experiences on the efficacy and safety of sequential ciclosporin and vedolizumab therapy using a different therapeutic scheme to that reported by the Chicago Inflammatory Bowel Disease Center.

In our institution, for steroid-refractory ulcerative colitis, we prefer to use induction therapy with intravenous ciclosporin followed by oral administration, usually continuing until week 52 or until the occurrence of the first unbearable side effect. Although short-term efficacy of ciclosporin is unquestionable, side effects are common and so an effective drug with better safety profile is needed to maintain remission. Previously, we chose infliximab for this purpose,[2] however, currently vedolizumab is more frequently selected.[3] Of 21 ulcerative colitis patients who were treated with both ciclosporin and vedolizumab at our centre, 13 received sequential therapies. Data of these 13 ulcerative colitis patients who were transitioned from intravenous to oral ciclosporin in combination with vedolizumab between January 2016 and May 2020 were analysed. The first vedolizumab infusion was given two weeks after starting ciclosporin.

We followed patients up for a median of 20.7 months (range 3-24 months). Three patients had left-sided colitis and 10 patients had extensive colitis. Colectomy-free survival rates were 100% throughout the periods. The median partial Mayo score decreased from 6 to 1 at week 14 (P = 0.003), and to 0 at week 52 (P = 0.011). Eleven patients (85%) achieved clinical remission at week 14 and steroid-free remission rate was 54% at that time. All of the patients followed up to 52 weeks were in clinical remission at that point, and the steroid-free remission rate was 63%. Decrease in baseline CRP was not significant either at week 14 (median 8.5 μg/mL to 6.2 μg/mL, P = 0.98), or at week 52 (to 2 μg/mL, P = 0.23). Sixty-two percent of patients were still on ciclosporin at week 14, and 50% at week 52. At the time of most recent follow-up, 77% of the patients are still on vedolizumab.

We observed tonsillitis and slight urea elevation as adverse effects in two patients and both were associated with ciclosporin use. Side effects were mild and ceased after stopping ciclosporin.

Our results confirm the observation of Ollech et al that induction therapy with ciclosporin transitioned to vedolizumab is a safe and effective way in acute, refractory ulcerative colitis. There is unmet need for a randomised trial to determine the optimal length of ciclosporin therapy using this strategy.

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Letter: early TIPSS in acute variceal bleed—debate continues

We read with great interest the article by Dunne et al[1], a randomised clinical trial (RCT) to assess the role of an early TIPSS in cirrhotic patients with variceal bleeding at high risk of treatment failure and death. The study was designed to validate the results of a previously published multicentre RCT from Europe.[2] The authors in this study report that patients with early TIPSS had no difference in survival and variceal rebleeding rates, as compared to standard of care. On per-protocol analysis, the early TIPSS group had no survival benefit, the rates of variceal bleeding were less, while rates of hepatic encephalopathy were more. The authors highlight the fact that early TIPSS (within 72 hours) is often not possible due to logistic issues, which led to the early closure of this study.