Simultaneous inhibition of $\alpha 4/\beta 7$ integrin and tumour necrosis factor- α in concomitant spondyloarthritis and inflammatory bowel disease

We read with interest the article by Varkas *et al*¹ suggesting a temporal association between the initiation of vedolizumab (VDZ) for inflammatory bowel disease (IBD) and induction or worsening of spondyloarthritis (SpA). This suggests that in patients with IBD, there may be limited efficacy of $\alpha 4/\beta 7$ integrin blockade for management of extraintestinal manifestations, particularly for arthritis and sacroiliitis.^{2,3} Treatment of SpA in subjects on VDZ for associated IBD is highly challenging for the treating physician. We describe below two patients who were treated with a combination treatment of VDZ and certolizumab pegol (CZP) (table 1).

Patient 1 is a 24 year-old man diagnosed with juvenile-onset SpA in 2008 and Crohn's disease (CD) in 2011. Sequential treatments with numerous tumour necrosis factor (TNF)- α inhibitors were associated with loss of efficacy or intolerance. In 2014, initiation of CZP was able to control articular symptoms. During follow-up, he developed uncontrolled disease activity of his CD, and in 2016 it was decided to add VDZ to the CZP treatment. Excellent responses of both gastrointestinal and musculoskeletal symptoms were noted. After 10 months of ongoing combination therapy, the patient is still without any symptoms of either IBD or SpA. No adverse events were reported.

Patient 2 is a 48 year-old woman diagnosed with ulcerative colitis (UC) in 2012. After inadequate response to numerous TNF- α inhibitors, she was initiated on VDZ. Despite good clinical and endoscopic response of her colitis, she developed inflammatory back pain, peripheral arthritis and enthesitis 5

months following the initiation of VDZ. A pelvic MRI confirmed bilateral sacroiliitis. CZP was initiated in lieu of VDZ to provide adequate control of the arthritis. Nine months after the last infusion of VDZ, the patient presented with a flare of UC. It was then decided to reinstate VDZ in addition to CZP. After the fourth infusion of VDZ, recurrence in the symptoms of arthritis was noted, and it was decided to discontinue CZP given its loss of efficacy. No adverse events were reported neither during the time of combination therapy nor following its cessation.

In spite of a relatively short follow-up, it is reassuring that no serious adverse events or infectious complications were recorded in our patients. Sustained remission was observed in patient 1, whereas recurrence of arthritis was observed in patient 2. Our report suggests that combination of VDZ and TNF- α could be considered in the therapeutic armamentarium for patients with SpA and IBD. Previous reports similarly showed no increased safety signals⁴⁻⁶; however, larger studies are needed in order to assess the outcomes of simultaneous inhibition of $\alpha 4/\beta 7$ integrin and TNF- α .

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Table 1 Patient characteristics, treatment and outcome of subjects treated with VDZ and CZP combination therapy

	Patient 1	Patient 2
Age (years)	24	48
Sex	Male	Female
Ethnicity	Caucasian	Caucasian
HLA-B27	Negative	Negative
Family history	Positive	Negative
Modified New York criteria*	Yes	No
Age at SpA onset (years)	15	47†
Age of onset of IBD (years)	21	43
Biologic use prior to combination therapy	GOL, IFX, ADA, CZP	IFX, ADA, GOL, VDZ, CZP
Reason for combination therapy	Active colitis‡	Active colitis‡
Treatment	VDZ+CZP	VDZ+CZP
Duration of follow-up (months)	10	3.5
Infections	None	None
Outcome	Remission	Flare of SpA

*Sacroiliitis $\geq$ bilateral grade 2 or unilateral grade 3.

†Symptoms onset 5 months following initiation of VDZ.

‡Despite adequate control of SpA on CZP.

ADA, adalimumab; CZP, certolizumab pegol; GOL, golimumab; HLA, human leucocyte antigen; IBD, inflammatory bowel disease; IFX, infliximab; SpA, spondyloarthritis; VDZ, vedolizumab.