Response to: 'Simultaneous inhibition of $\alpha 4/\beta 7$ integrin and tumor necrosis factor- α in concomitant spondyloarthritis and inflammatory bowel disease' by Richard *et al*

We thank Dr Richard *et al* for their interest in our work and the communication of their experiences in daily practice.¹ In patients affected with both spondyloarthritis (SpA) and refractory inflammatory bowel disease (IBD) despite anti-tumour necrosis factor (TNF) therapy, treatment options are limited. While anti-TNF therapy has shown remarkable efficacy in the treatment of both axial and peripheral SpA, even long term, the results in IBD were less satisfying.^{2,3} With the introduction of vedolizumab, a new mode of action and hope for refractory patients was installed.^{4,5} Nevertheless, as we reported earlier, vedolizumab did not show any efficacy in a series of patients with SpA and might even induce SpA-like disease in certain individuals.⁶

Richard *et al* describe the use of certolizumab pegol in combination with vedolizumab in two patients with IBD refractory to anti-TNF. Interestingly, while patient 1 represents the lack of efficacy of vedolizumab in SpA, unfortunately patient 2 matches the profile of patients developing SpA with the initiation of vedolizumab.

Although we agree that the combination of drugs is inevitable in these particular cases, several practical implications arise. First, which anti-TNF should be preferred and when should it be installed? In these cases, anti-TNF therapy has failed to confine gut inflammation. Therefore, the use of monoclonal antibodies for treatment of extra-articular manifestations may be redundant, unless other EAMs such as psoriasis or uveitis occurred in the disease course. Additionally, in the combination of two biological immunosuppressive agents safety is a key determinant. This has particularly been a point of concern when combining biologics in patients with rheumatoid arthritis.⁷ Therefore, the use of etanercept with shorter half-life may be preferred in these patients developing SpA after vedolizumab treatment.⁸ However, in patients already diagnosed with both SpA and IBD, the anti-TNF therapy will usually be withdrawn before initiation of vedolizumab due to inefficacy. This could increase the risk of secondary inefficacy of anti-TNF due to immunogenicity when reinstated for SpA. This presumably may have been the case in patient 2. Thus, in case of predictable flare of SpA in patients displaying both diseases, the withdrawal of anti-TNF should be avoided. However, at present there are no clear predictors available that permit to predict which patients will develop new onset SpA or a relapse on initiation of vedolizumab.

Second, there are also questions regarding reimbursements by insurance companies or legislators. Unfortunately, both vedolizumab and anti-TNF therapy are expensive therapies. Although the medical need is urgent, the use of both drugs in the same patients is at present based on expert opinion and therefore not necessarily reimbursed. Eventually, outcome and safety data might persuade legislators to embed this treatment strategy in general practice. However, for now, rheumatologists and gastroenterologists might have to rely on medical need programmes to treat their patients accordingly.

Therefore, the use of vedolizumab monotherapy after loss of efficacy of anti-TNF at the level of the gut in patients displaying

both SpA and IBD should be taken with caution as flares may be expected short term. Additionally, in patients developing SpA-like disease after treatment with vedolizumab, for now, combination therapy with anti-TNF might be inevitable. There is currently little evidence that vedolizumab should be preferred over anti-TNF therapy in biologic-naïve patients. Although several case reports have reported on short-term effects, long-term evaluation should be conducted to determine the safety of such a dual strategy on malignancy and infectious complications.

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REFERENCES

- 1 Richard N, Hazel EM, Haroon N, *et al*. Simultaneous inhibition of $\alpha 4/\beta 7$ integrin and tumour necrosis factor- α in concomitant spondyloarthritis and inflammatory bowel disease. *Ann Rheum Dis* 2018;**77**:e86.
- 2 Stidham RW, Lee TC, Higgins PD, *et al*. Systematic review with network meta-analysis: the efficacy of anti-tumour necrosis factor- α agents for the treatment of ulcerative colitis. *Aliment Pharmacol Ther* 2014;**39**:660–71.
- 3 Hazlewood GS, Rezaie A, Borman M, *et al*. Comparative effectiveness of immunosuppressants and biologics for inducing and maintaining remission in Crohn's disease: a network meta-analysis. *Gastroenterology* 2015;**148**:344–54. quiz e14–5.
- 4 Sandborn WJ, Feagan BG, Rutgeerts P, *et al*. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med* 2013;**369**:711–21.
- 5 Feagan BG, Rutgeerts P, Sands BE, *et al*. Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2013;**369**:699–710.
- 6 Varkas G, Thevissen K, De Brabanter G, *et al*. An induction or flare of arthritis and/or sacroiliitis by vedolizumab in inflammatory bowel disease: a case series. *Ann Rheum Dis* 2017;**76**:878–81.
- 7 Weinblatt M, Combe B, Covucci A, *et al*. Safety of the selective costimulation modulator abatacept in rheumatoid arthritis patients receiving background biologic and nonbiologic disease-modifying antirheumatic drugs: a one-year randomized, placebo-controlled study. *Arthritis Rheum* 2006;**54**:2807–16.
- 8 van Darter SA, Fransen J, Kievit W, *et al*. Difference in the risk of serious infections in patients with rheumatoid arthritis treated with adalimumab, infliximab and etanercept: results from the Dutch Rheumatoid Arthritis Monitoring (DREAM) registry. *Ann Rheum Dis* 2013;**72**:895–900.