

Dear Editor

We thank Dr. Jamilloux and colleagues for their insightful comments and also for their engagement in the FOCUS project. We are pleased that they continue to be in accord with the tenet and outputs of the work in FOCUS.

The authors raise three general points with which we agree. Firstly, the authors comment on the important conundrum of which TNF inhibitor to use, particularly with respect to acute anterior uveitis (AAU) and spondyloarthropathies if prevention of uveitis is a goal. A recent Swedish registry promulgates the discussion by demonstrating superiority of antibodies over soluble inhibitors for preventing AAU occurrences¹. This is consistent with the recommendation in our report if a biologic is selected. We thank the authors for pointing out that there are other routes to prevention of B27+ AAU associated with systemic disease in particular and such routes are gaining increasing levels of evidence.

Secondly, with respect to their comments on the VISUAL trials design not replicating 'standard' practice, the data nevertheless remain in support of strong biological and clinical efficacy. The VISUAL studies have generated robust high-level evidence to support the FOCUS group statements, but the studies implicitly (which was not discussed in the article) highlight further evidence gaps. These include a comparator to response to other immunomodulators. We also require additional study on the most appropriate patient group(s) of uveitis patients to treat. To that end, we are thankful for an opportunity to clarify. We did comment in the article: "optimizing the dosage of the noncorticosteroid systemic agent often is the first option before introducing a novel medication or approach" and elsewhere we endorse the option to consider a second conventional immunosuppressive before a biologic. We thus agree broadly with the comments made and endorse the approach in severe disease, such as Behcet's disease, to rapidly escalate to biologic therapy to deliver a rapid remission. Notwithstanding, VISUAL studies have resulted in the UK National Institute for Health and Care Excellence (NICE) technology appraisal guidance to recommend commissioning of adalimumab through NHS England for treatment of bilateral, active sight-threatening disease and refractory (or intolerant) to one immunomodulatory. Behcet's disease has separate commissioning arrangements for early biologic use if indicated.

Thirdly, the morbidity of 'biologic' use is a significant concern. An update from the original data published from the 2009 SITE data which they cite is awaited. We have to be wary of lumping adalimumab with all biologics when determining morbidity risk. Certainly the underlying disease might influence the safety of a biologic. Nonetheless, it is reassuring that an assessment of more than 23,000 subjects enrolled in clinical trials over 12 years for more than a dozen indications demonstrates that subjects receiving adalimumab enjoyed a statistically significant reduction in the standardized mortality rate (G. Burmester et.al., presented at the 2017 meeting of the American College of Rheumatology, San Diego). Whatever the new data bring, the discussion with patients should include note of their past history (e.g especially cancer history) to weigh risk:benefits appropriately.

REFERENCES

1. Lie E, Lindström U, Zverkova-Sandström T, Olsen IC, Forsblad-d'Elia H, Askling J, Kapetanovic MC, Kristensen LE, Jacobsson LTH. Tumour necrosis factor inhibitor treatment and occurrence of anterior uveitis in ankylosing spondylitis: results from the Swedish biologics register. *Ann Rheum Dis*. 2017; Sep;76(9):1515-1521.