Reply to the letter from Braun et al.

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We thank the correspondents for their interest and valuable comments [1,2]. We agree that ankylosis of the sacroiliac joints is not the disease process that has most functional impact on patients, but we have published our observations as sacroiliitis can be regarded as a potential model for joint disease in patients with spondyloarthritis. As commented, the progression of ankylosis in an adolescent population has not been previously described, and these observations add to the understanding of disease course even when biologic therapies are prescribed. It is interesting that some patients who received biologic treatment for many years were not completely protected from bony ankylosis despite a reduction in bone osteitis. Our data did not allow us to examine whether treatment reduced or otherwise influenced the rate of progression in these patients; rather, the results show that biologic therapy – prescribed in a 'real-world' setting in an early spondyloarthritis cohort - does not entirely prevent structural progression. We agree that it would have been optimal to initiate therapy in these patients sooner after diagnosis. However, there were several factors contributing to the delay in prescription of biologic therapies. In our institution, the clinical practice has been for patients with enthesitis-related arthritis (ERA) to undergo a six month trial of conventional DMARDs/NSAIDs, especially if there is evidence of peripheral joint involvement. This is supported by some evidence that ERA patients may respond to conventional DMARDs [3]. If there is no clinical response coupled with MRI evidence for sacroiliitis, patients are then considered for biologic therapy. Delays can also be exacerbated by issues specific to adolescent patients, such as school exams and family holidays. Our study was retrospective and consequently we do not have full clinical and biomarker data on our cohort. As per current guidelines for juvenile idiopathic arthritis, patients have been able to continue biologic treatment only if there was evidence of clinical response [4]. A prospective study with full imaging and clinical documentation would be ideal. However, obtaining funding to support a non-interventional, observational study has not been possible so far and may be inhibited by the overarching focus of funding bodies on the development of new immunotherapies or more holistic approaches to patient care, rather than imaging per se. MRI, and in particular quantitative MRI, does offer a real opportunity to observe and quantify inflammation and disease course in inflammatory arthritis in an objective fashion [5–8]. Although, as the correspondents comment, clinical response to therapy remains the aim of disease treatment, clinical evaluation as a disease assessment tool has many confounders and limitations [9]. Clinical evaluation is particularly problematic in adolescent cohorts, where pain is multifactorial and clinical disease scores may be heavily confounded by noninflammatory factors. Additionally, age-tailored disease activity scores for adolescent population have only recently been validated [10]. Looking forward, MRI has the potential to be more specific for inflammation than either clinical assessment of disease or serum biomarkers of inflammation, particularly as new MRI techniques come into practice. It has the potential to support clinical therapeutic studies, and by demonstrating evidence of active disease, it can contribute to developing understanding of the role of inflammation in the evolution of new bone formation and disease progression. Our study is a small part of developing

that understanding, and we look forward to the integration of imaging into future studies on disease mechanism.

## References

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