Response to: Correspondence on 'No efficacy of anti-IL-23 therapy for axial spondyloarthritis in randomised controlled trials but in post-hoc analyses of psoriatic arthritis-related 'physician-reported spondylitis'?' by Braun and Landewe

With great interest, we read the comment of our colleagues from the UK on our recent viewpoint,¹ and we appreciate that they largely agree with us.² This is a bit different in a recent review on the same topic,³ which argues that it is still possible that anti-IL23 agents work for axial psoriatic arthritis (PsA). Nevertheless, our colleagues from the UK raise two important points, which we like to shortly comment on.

First, the important factor of age is discussed, which plays an important role in the frequent clinical situation of patients presenting to the doctor because of acute or chronic back pain—simply because the prevalence of degenerative changes in the axial skeleton does increase with age,^{4,5} and axial spondyloarthritis (axSpA) starts most often in the third decade of life⁶—the reason why the classification criteria for axSpA have age at onset <45 years in the first row.⁷ Nevertheless, late-onset SpA does reportedly occur.⁸

However, patients with PsA are usually older when their disease starts,⁹ which simply increases the likelihood of degenerative changes in the spine to take place. In addition, neither axSpA nor PsA patients at any age are protected from such changes,^{10,11} and even in patients with these diagnoses, different reasons for explaining the presenting symptom of back pain come into the important workup of excluding differential diagnoses.¹² Indeed, in one study, degenerative changes were more likely to explain the source of back pain in patients with axSpA than inflammatory changes.¹³ In relation to the discussion on axSpA and axial PsA being different or even representing different diseases, which may or may not respond differently to medication based on inhibition of IL-23, we find it most important that in all post hoc analyses published so far included that patients were not treated because of back pain but because of peripheral arthritis, and given, that the Bath Ankylosing Spondylitis (AS) Disease Activity Index (BASDAI) is not an axSpA-specific instrument¹⁴—even though developed for AS—the slight bystander decrease noted is by far not sufficient to promote efficacy on axial inflammation due to which disease whatsoever.

This statement is closely connected to the second point brought up by our colleagues, which contains the important advice that in a clinical situation of a patient with PsA and back pain, the presence of the latter should not be considered to be a contraindication for anti-IL23 therapy. We agree with that—as long as the source of back pain is not clear. If axial inflammation has been detected - as it is possible by magnetic resonance imaging (MRI) - we would still prefer other compounds with proven efficacy for axial inflammation in axSpA.

Finally, we like to stress that our understanding of the current discussion is that there is little doubt that there is no major difference between AS with and without psoriasis—with HLA B27 playing a major role as a severity factor.¹⁵ However, the new classification of non-radiographic (nr-)axSpA brings a situation of nr-axSpA with and without psoriasis, which may be considered differently because of the increasing uncertainty with minor MRI lesions in the sacroiliac joints (SI) joints as an important factor, because of strong evidence that minor MRI lesions can be

found in other clinical situations and even in the population.^{16,17} There are two ongoing initiatives, which are likely to shed more light on this discussion: the Classification of axSpA Inception Cohort (CLASSIC) and the Axial Involvement in PsA Cohort (AXIS) study organised by Assessment of Spondyloarthritis International Society (ASAS) and the second together with Group for Research and Assessment of Psoriasis and PsA (GRAPPA).¹⁸

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