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 Landewé

We read with interest the Viewpoint article by Braun and Landewé¹ regarding post-hoc analysis of back pain in trials of interleukin (IL)-23 inhibitor therapy in patients with peripheral psoriatic arthritis (PsA). Indeed, we share their concerns regarding study design, the use of outcome measures developed for axial spondyloarthritis (axSpA) and, most importantly, the attribution of the diagnostic label 'physician-reported spondylitis' in these patients. In addition to the issues eloquently outlined in the article, it is important to be aware that the pre-test probability of inflammatory disease being directly responsible for back pain is likely much lower in patients with PsA who are older and therefore more likely to have mechanical or non-specific back pain than people presenting with axSpA. In other words, even before doing any test, a middle-aged person with PsA, as represented in most phase III PsA clinical trials, is more likely to have non-inflammatory than inflammatory back pain. These 'causes' of back pain do of course co-exist and are not easily distinguished by clinical or imaging assessments. For example, disc and degenerative spinal disease can lead to apparent inflammatory features, such as bone marrow oedema, on MRI^{2,3} that are likely a secondary response to altered biomechanical stresses rather than primary inflammatory disease and therefore unlikely to be responsive to biologic therapies. Furthermore, imaging data on the prevalence and natural history of spinal involvement in PsA are limited. We therefore agree that more research is required to both define inflammatory axial involvement in PsA (for which global initiatives are ongoing, as outlined by Braun and Landewé) and evaluate the effect of specific therapies on this component of psoriatic disease. The latter will need to be tested in appropriately recruited PsA populations and will likely require comparison between active therapies with similar efficacy in both peripheral joint and skin disease to mitigate for the bystander effect resulting from improvements in these non-axial domains.

However, until this is resolved, clinicians are faced with a dilemma when choosing a biologic therapy for patients with PsA with significant spinal symptoms. Indeed, where spinal symptoms are the sole or dominant musculoskeletal complaint in a person with psoriasis, there is clearly a requirement to determine, as far as possible, whether or not there is likely to be active inflammatory axial disease to warrant biologic therapy. This should be done using a combination of clinical, imaging and laboratory assessment, while also taking into account context and likelihood. However, in patients with PsA with spinal symptoms who also have significant active peripheral joint disease that warrants biologic therapy in its own right, should IL-23 inhibitors be avoided on the basis of the negative data from for these agents in axSpA trials?^{4,5} For now, we believe that in light of the difficulty in determining the nature of the axial involvement in PsA, treatment decisions should be based on considerations relating to peripheral musculoskeletal disease, extent of cutaneous psoriasis, previous therapies, extra-articular manifestations, comorbidities and safety to select the most appropriate therapy for these patients. While we agree with Braun and Landewé that the current post hoc analyses do not prove that

IL-23 inhibitors are efficacious for inflammatory axial disease in PsA, we suggest that, until further robust evidence is available, the presence of axial symptoms, whether inflammatory or non-inflammatory, should not be considered a reason to avoid IL-23 inhibitor therapy, if that is perceived to be otherwise the most appropriate and safest choice for that individual's peripheral musculoskeletal and cutaneous disease.

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REFERENCES

- Braun J, Landewé R. 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'? *Ann Rheum Dis* 2021.
- Tsoi C, Griffith JF, Lee RKL, et al. Imaging of sacroiliitis: current status, limitations and pitfalls. *Quant Imaging Med Surg* 2019;9:318–35.
- Berthelot J-M, le Goff B, Maugars Y, et al. Sacroiliac joint edema by MRI: far more often mechanical than inflammatory? *Joint Bone Spine* 2016;83:3–5.
- Deodhar A, Gensler LS, Sieper J, et al. Three multicenter, randomized, double-blind, placebo-controlled studies evaluating the efficacy and safety of ustekinumab in axial spondyloarthritis. *Arthritis Rheumatol* 2019;71:258–70.
- Baeten D, Østergaard M, Wei JC-C, et al. Risankizumab, an IL-23 inhibitor, for ankylosing spondylitis: results of a randomised, double-blind, placebo-controlled, proof-of-concept, dose-finding phase 2 study. *Ann Rheum Dis* 2018;77:1295–302.