Response to: 'Correspondence on 'Effectiveness of secukinumab versus an alternative TNF inhibitor in patients with axial spondyloarthritis previously exposed to TNF inhibitors in the Swiss Clinical Quality Management cohort' by Micheroli *et al*' by Huang *et al*

Adrian Ciurea , **Raphael Micheroli**

Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland

Correspondence to Professor Adrian Ciurea, Department of Rheumatology, University Hospital Zurich, Zurich CH-8091, Switzerland; adrian.ciurea@usz.ch

Handling editor Josef S Smolen

Funding The original study discussed in this correspondence was supported by a research grant from Novartis.

Competing interests AC has received consulting and/or speaking fees from AbbVie, Celgene, Eli Lilly, Merck Sharp & Dohme, Novartis and Pfizer, outside the submitted work. RM has received consulting and/or speaking fees from Gilead, Eli Lilly and AbbVie, outside the submitted work.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

To cite Ciurea A, Micheroli R. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2020-218832

Received 17 August 2020
Accepted 18 August 2020

Linked

► http://dx.doi.org/10.1136/annrheumdis-2020-218779

Ann Rheum Dis 2020;**0**:1. doi:10.1136/annrheumdis-2020-218832

ORCID iD
Adrian Ciurea http://orcid.org/0000-0002-7870-7132

We would like to thank Huang *et al*[1] for their interest in our study[2] and the opportunity to discuss some aspects in more detail.

The limited sample size precluded subgroup analyses with regard to either the type of tumour necrosis factor inhibitor (TNFi) agent or the reason for discontinuation of the previous biologic disease-modifying antirheumatic drug (bDMARD). Moreover, drug discontinuation might be due to a combination of reasons (eg, only partial effectiveness combined with otherwise acceptable adverse events (AE)) further impeding this type of analysis in a real-world setting and requiring the definition of a hierarchy of reasons for discontinuation as introduced in a previous study.[3]

We have used two different statistical methods to account for potential confounding by indication. A total of 16 covariates were incorporated in both propensity score-based analyses as well as covariate adjustment, with a particular focus in avoiding collinearity between variables. Given the observational nature of our study, we cannot entirely exclude residual confounding. However, the numerical higher rate of infection in patients treated with secukinumab (SEC) should not be interpreted as an indication of residual confounding, as the exact nature of AE leading to drug discontinuation was not known in 47% of patients.

The choice of our outcomes was informed by current international treatment recommendations in real-world settings.[4] We have preferred a reduction in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) by 50% over the achievement of the 20% and 40% improvement criteria defined by the Assessment of Spondylo Arthritis international Society (ASAS20 and ASAS40, respectively), as it is more intuitive to assess response in day-to-day clinical practice. According to guidelines, continuing a bDMARD in axial spondyloarthritis (axSpA) should be considered if after at least 12 weeks of treatment a BASDAI improvement of at least 2 points or an improvement in the Ankylosing Spondylitis Disease Activity Score (ASDAS) of at least 1.1 points is achieved.[4] Given their clinical relevance, both outcomes were included in our study, as was the proportion of patients reaching an ASDAS <2.1. We do not recommend comparing endpoints between studies with different design, inclusion criteria and treatment in different calendar periods.

A superiority of interleukin-17 (IL-17) inhibitors in TNFi-naïve versus TNFi-experienced patients was indeed demonstrated for both SEC and ixekizumab.[5–7] There is no inconsistency with the results of our study, as the latter focused exclusively on TNFi-experienced patients.

Missing data precluded a formal comparison of specific AE rates between SEC and TNFi, as already mentioned. With regard to the two patients with paradoxical psoriasis during SEC treatment, this AE had already occurred during previous TNFi treatment in both patients and failed to improve during SEC. New onset of psoriasis induced by SEC in patients with axSpA has also been described and its pathogenesis remains largely unknown.[8 9]

A significant proportion of patients with axSpA did not respond adequately to both TNF and IL-17 inhibition and we agree with Huang *et al* that investigation of additional modes of treatment action is warranted.

REFERENCES

1 Huang J-X, Leong P-Y, JC-C W. Correspondence on "Effectiveness of secukinumab versus an alternative TNF inhibitor in patients with axial spondyloarthritis previously exposed to TNF inhibitors in the Swiss Clinical Quality Management cohort" by Micheroli R et al. *Ann Rheum Dis* 2020.10.1136/annrheumdis-2020-218779
2 Micheroli R, Tellenbach C, Scherer A, *et al*. Effectiveness of secukinumab versus an alternative TNF inhibitor in patients with axial spondyloarthritis previously exposed to TNF inhibitors in the Swiss Clinical Quality Management cohort. *Ann Rheum Dis* 2020;1209. doi:10.1136/annrheumdis-2019-215934.
3 Ciurea A, Exer P, Weber U, *et al*. Does the reason for discontinuation of a first TNF inhibitor influence the effectiveness of a second TNF inhibitor in axial spondyloarthritis? results from the Swiss clinical quality management cohort. *Arthritis Res Ther* 2016;18:71.
4 van der Heijde D, Ramiro S, Landewé R, *et al*. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis* 2017;76:978–91.
5 Sieper J, Deodhar A, Marzo-Ortega H, *et al*. Secukinumab efficacy in anti-TNF-naive and anti-TNF-experienced subjects with active ankylosing spondylitis: results from the measure 2 study. *Ann Rheum Dis* 2017;76:571–92.
6 van der Heijde D, Cheng-Chung Wei J, Dougados M, *et al*. Ixekizumab, an interleukin-17A antagonist in the treatment of ankylosing spondylitis or radiographic axial spondyloarthritis in patients previously untreated with biological disease-modifying anti-rheumatic drugs (COAST-V): 16 week results of a phase 3 randomised, double-blind, active-controlled and placebo-controlled trial. *Lancet* 2018;392:2441–51.
7 Deodhar A, Poddubnyy D, Pacheco-Tena C, *et al*. Efficacy and Safety of Ixekizumab in the Treatment of Radiographic Axial Spondyloarthritis: Sixteen-Week Results From a Phase III Randomized, Double-Blind, Placebo-Controlled Trial in Patients With Prior Inadequate Response to or Intolerance of Tumor Necrosis Factor Inhibitors. *Arthritis Rheumatol* 2019;71:599–611.
8 Currado D, Margiotta D, Conforti C, *et al*. New onset of psoriasis induced by secukinumab in a patient with ankylosing spondylitis: a case report. *Scand J Rheumatol* 2020;49:75–6.
9 Durmaz K, Ataseven A, Ozer I. Paradoxical plaque psoriasis due to secukinumab treatment in an ankylosing spondylitis patient. *Dermatol Ther* 2020:e13504.