Confirmation on the immunogenicity assay used in the SB4 phase III study: response to the comments by Meacci *et al*

We appreciate Meacci *et al*[1] for the comments on the anti-drug antibody (ADA) detection methods.

As noted by Meacci *et al*, the Meso Scale Discovery (MSD) electrochemiluminescence (ECL) bridging assay (Maryland, USA) was used in the SB4 Phase III study to detect ADAs.[2] The bridging assay format relies on the characteristics of ADA to crosslink two drug molecules conjugated to a capture and a detection label. Due to the methods employed in the ECL bridging technology, ECL is more sensitive and has higher drug tolerance compared with ELISA or surface plasmon resonance assay.[3 4] Furthermore, in order to facilitate detection of ADA, the drug-ADA immune complexes in our study samples were dissociated through acid dissociation,[4] leading to an improved drug tolerance.

According to the biosimilar guidelines[5–7] the goal of the clinical immunogenicity assessment is to evaluate potential differences between the proposed product and the reference product in the incidence and severity of human immune responses. It is recommended that the sponsor should use assays that are sensitive and capable of detecting all antibodies induced against the product in all antibody-positive patients. For the reasons explained above, ECL was employed in our study as well as most of other biosimilar studies[8–11] to detect any difference in immunogenicity between the biosimilar and reference product. Overall, as pointed out by Meacci *et al*, the use of ECL may have contributed to the higher incidence of ADA in our study compared with main literature data.[12–14]

We hope that the details and confirmation on the assay methods provide the readers of Annals of the Rheumatic Diseases additional reference for the immunogenicity data in our study.

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