Anti Etanercept and anti SB4 antibodies detection: impact of the assay method

We would like to underline the fundamental role of the assay method used to detect anti-drug antibodies. In Emery *et al*'s article¹ a very high percentage of patients show anti-etanercept (ETN) antibodies, 13.1%, which is much higher compared with main literature data, reporting generally less than 5% incidence.^{2–5} This apparent discrepancy can be explained by the different technical findings of laboratory methods employed in the works. Emery *et al* employs electrochemiluminescence method (ECL), while most of the authors performed assays on ELISA or Radio Immuno Assay (RIA) platforms. The diagnostic performances of these methods are very dissimilar.

ECL is known to have characteristics of excellent sensitivity, high drug tolerance, and minimal influence of sample matrix.⁶ Furthermore, Emery *et al*'s work serum samples were subjected to acid treatment before the analysis to increase the anti-drug antibodies recovery.

RIA and ELISA methods have a lower sensitivity and are subjected to drug interference, even though an acid pretreatment of sample can be performed. However, they are much more widely employed worldwide, since they are more standardised and user-friendly than ECL. All these findings could justify the substantial difference in anti-ETN antibodies recovery by ECL, when compared with other methods.

Interestingly, in the Emery *et al*'s work, only 0.7% of patients had anti-SB4 antibodies. Since in the ECL method the tagged drug (ETN or SB4) is directly used in a single-step assay,⁷ the capability of the assay to detect anti-ETN or anti-SB4 could be identical. Nevertheless, because of the great impact of such new results on clinical management, as also underlined by Moots *et al*,⁸ it would be very interesting to study in depth the different immunogenicity of these two drugs found in the cited study. In particular, some more details on the confirmatory test results to evaluate the specificity of detected ADAs, would be clarifying. A very recently published report comparing the immunogenicity of ETN and biosimilar HD203, found ADAs in 8/147 patients taking HD203 and in 3/147 patients taking ETN.⁹ So further studies are needed to better understand factors contributing to different immunogenicity of SB4 than ETN, with a bigger number of patients.

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