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Response to Dr. Martaan Boers' eLetter: "Let's stop fooling ourselves. In RA, only ACR/EULAR criteria define remission and equate with absence of disease!"

Dear Editor,

We would like to thank Dr Boers for his critical comments on our study raised in his eLetter,[1] and address his concerns regarding our manuscript.

Firstly, we would like to emphasize that we are in support of the statements in the guidelines issued by ACR/EULAR in early 2011,[2] and acknowledge that the DAS28(ESR)-based definition of clinical remission (DAS28[ESR] <2.6) is less stringent than the SDAI definition.

However, our manuscript does not make any claims that DAS28(ESR)-based remission is reflective of 'true' or 'real' remission or the absence of disease. Our methods and figures state clearly that our study used the DAS28(ESR)-based remission criterion. Furthermore, the manuscript also reports the proportion of patients who achieved SDAI remission (please see Figure 4A in the paper) as a secondary endpoint, which was statistically significant between CZP + MTX treated and PBO+MTX-treated groups at $p<0.001$.[3]

The protocol for the C-EARLY study was developed prior to the issue of the 2011 ACR/EULAR guidelines. At this time in 2010, DAS28(ESR) <2.6 was still acknowledged as both a validated and clinically-relevant definition of disease remission for treatment with biological DMARDs.[4,5] In our study, we clearly define sustained remission as DAS28(ESR) <2.6 at both Weeks 40 and 52. Maintenance of disease remission is a highly relevant clinical goal for patients with chronic disease. However, it is rarely used in clinical trials because it is difficult to achieve. Despite this, we employed sustained disease remission as our primary endpoint in C-EARLY. This endpoint was not chosen because it was easy to achieve; it was chosen for its high level of stringency and relevance to patient care.

The C-EARLY study was designed to have an additional, extended component (NCT01521923),[6] which evaluated the efficacy and safety of either stopping, continuing, or reducing the frequency of CZP dosage over an additional year (Weeks 52–104). An important component for C-EARLY Period 2 was the evaluation of disease flares. To ensure standardisation of the definition a flare, we followed the OMERACT RA flare guidelines, which uses changes in DAS28(ESR) scores to evaluate disease worsening.[7] In order to maintain consistency and the ability to evaluate disease activity with clinical targets such as LDA and remission, we used DAS28(ESR)-based definitions in both periods of the C-EARLY study as primary endpoints.

We agree with Dr Boers that the SDAI-based definition of remission now supersedes the previous DAS28(ESR)-based standard and we support the statement that future clinical trials in rheumatoid arthritis should adhere to the recommendations issued by ACR and EULAR.

Yours sincerely,

Paul Emery

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