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

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.[2]

First, we would like to emphasise that we are in support of the statements in the guidelines issued by the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) in early 2011,[3] and acknowledge that the Disease Activity Score 28 erythrocyte sedimentation rate (DAS28(ESR)) based definition of clinical remission (DAS28(ESR) <2.6) is less stringent than the simple disease activity index (SDAI)- and Boolean-based definitions.

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-based remission (please see figure 4A in the paper) as a secondary endpoint, which was achieved by more certolizumab pegol (CZP)+methotrexate (MTX) treated patients than placebo (PBO)+MTX-treated patients ($p<0.001$ [nominal p-value]).[2]

The protocol for the certolizumab pegol effective in early rheumatoid arthritis (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 disease-modifying antirheumatic drugs.[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. Furthermore, as previous RA trials have used DAS based measures of low disease activity (LDA) and remission, techniques such as meta-analyses can applied to compare the results described in our article with other published studies.

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 of a flare, we followed the Outcome Measures in Rheumatoid Arthritis Clinical Trials rheumatoid arthritis flare guidelines, which uses changes in DAS28(ESR) scores to evaluate disease worsening.[7] In order to maintain consistency between the two parts of the study, and 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- and Boolean-based definitions of remission now supersede the previous DAS28 (ESR)-based standard and we support the statement that, where appropriate, future clinical trials in rheumatoid arthritis should adhere to the recommendations issued by ACR and EULAR.

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