Editorial

Inclusion Criteria Based on DAS28 Score: Strength of Improvement Is Less Dependent on Baseline Disease Activity Than Expected

In the past decade much effort was directed toward the lowering of disease activity in patients with rheumatoid arthritis (RA) and the most optimal disease state: remission. The word "remission" is commonly used in oncology to define a health condition in which the signs and presence of malignant disease are absent after treatment. The fact that treatment of RA has also become more and more effective by starting therapy early in the disease, combining disease-modifying antirheumatic drugs and the use of biologicals, has stimulated rheumatologists to aim for remission as well. However, in contrast to a number of malignancies, RA can seldom be "cured" and most patients show relapse after stopping treatment[1,2]. Therefore, the aim of treatment in RA is directed toward a low disease activity state, most often defined as a Disease Activity Score 28 (DAS28) < 3.2 and the threshold for "remission" at DAS28 < 2.6[3].

Recently, new preliminary criteria for remission have been published in an effort to predict a halt of radiographic progression and a good functional outcome[4]. These new remission criteria were not taken into account in the study of Visman, *et al*[5], which primarily focused in the DAS28 as an outcome measure of remission.

The efficacy of treatment in order to reach this goal of low disease activity is related to the disease activity level before treatment: the higher the disease activity at the start, the more improvement that can be expected. Therefore in most randomized clinical trials (RCT) in RA the entry criteria are based on a high level of disease activity in order to show a measurable and, even more important, impressive improvement by the treatment or drug studied. The question is whether this high level of disease activity before treatment is necessary to reach the same level of disease activity after treatment as in the case of a lower threshold at entry.

Moreover, the fact that many RCT use a relatively high threshold of disease activity does not imply that this is the best way to treat patients in daily clinical practice. The difference is also based on the fact that other patient selection criteria, such as age, comorbidity, etc., used in RCT do not apply to daily clinical practice, except for contraindications for this treatment.

The question whether patients with high disease activity benefit more from treatment compared with patients who have lower disease activity is well addressed by Visman, *et al*[5]. Moreover, their study also provides insight into the data obtained in daily clinical practice of the use of a biological, adalimumab, in RA, in comparison to the data of several clinical trials.

The results of their study illustrate nicely that patients with a high baseline DAS28 (> 5.1, with a mean DAS28 of 6.1) and with a lower DAS28 (< 5.1, with a mean DAS28 of 4.1) show almost the same endpoint after 28 weeks of treatment: a mean DAS28 level of, respectively, 4.0 and 3.0 (Visman, *et al*, Table 3). The delta in mean disease activity scores after 28 weeks compared with baseline was only 1 and 2 points. The same decrease in DAS was observed in the several clinical trials described in their Tables 1 and 3: about 2 points, ending with a DAS28 score between 3.5 and 4.0 regardless of the higher or lower disease activity score at baseline. Moreover, the percentage of patients reaching a low disease activity state (DAS < 3.2) or remission (DAS < 2.6) did not differ significantly between the groups, 37% and 23%, respectively.

The delta between DAS28 at baseline and after 28 weeks of treatment is of course higher in the patients with the higher DAS at baseline but the disease state after treatment does not differ much (mean values at 28 weeks between 3.67 and 4.53). A minimal level of disease activity, such as DAS > 3, however, should be present in order to expect a significant improvement.

The most important conclusion of this study is that a high disease activity score at baseline does not necessarily predict a better outcome than a lower disease activity score after 28 weeks of treatment with a biological. This observation supports the fact that more patients should be considered eligible for treatment with in this case adalimumab, in daily clinical practice than estimated in the figures of RCT.

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See Effect of the application of trial inclusion criteria on the efficacy of adalimumab therapy in a RA cohort, *page 1884*