Letter

Response to the commentary 'Pooled indices to measure rheumatoid arthritis activity: a good reflection of the physician's mind'

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See related commentary by Aletaha, http://arthritis-research.com/content/8/1/102, related research article by Vander Cruyssen *et al*., http://arthritis-research.com/content/7/5/R1063, and related commentary by van Riel and Fransen, http://arthritis-research.com/content/7/5/189

The February issue of *Arthritis Research & Therapy* included a commentary by Aletaha [1] on a recent report from our group [2].

First, Aletaha states that evaluation of the 'physician's mind' is best performed in a study setting in which the physician is unaware that their clinical decision is part of the investigation. It should be noted that the analysis we reported [2] was a *post hoc* analysis on a cohort of patients with rheumatoid arthritis (RA) who began infliximab therapy within the context of an expanded access programme, and in which infliximab therapy was provided for free until reimbursement in 2002. In the initial protocol it was pre-specified that, from week 30 onward, patients with insufficient response to the therapy could receive an extra vial at each infusion. This decision had to be taken at week 22 and was based on the treating rheumatologist's appreciation of the patient's condition and disease activity. Because the analysis presented in our report was not planned for in the initial protocol, a *post hoc* amendment to the initial protocol for our analysis was approved by the ethical committee in 2004. Thus, at the time of the study, the physicians were unaware that their behaviour would be evaluated in a separate analysis.

Second, we should like to clarify that the components of the American College of Rheumatology (ACR) core set response score and the Disease Activity Score (DAS28) were known to the treating physician, but not the calculated values of the ACR core set response score and DAS28.

A third issue highlighted by Aletaha [1] and by Van Riel and Fransen [3] is that in our study more than 50% of patients did not receive a dose increase, even though those patients had a DAS28 score greater than 3.2, indicating moderate or high disease activity. It can therefore be questioned why physicians 'neglected' to treat their patients more aggressively. It should be noted that the patients included in the study had long-standing destructive disease (median disease duration 10 years) and had previously failed to respond to aggressive therapy, as reflected by a failure to respond to a median of four disease-modifying antirheumatic drugs. Infliximab therapy was for most patients the final therapeutic option at the time of the study, and for such individuals and their physicians moderate disease activity was acceptable, representing an improvement over their previous state. Sokka and Makinen [4] recently suggested that when more treatment options become available, lower levels of RA disease activity will be required. Also, it should be mentioned that the study was a reflection of real life practice for an important number of rheumatologists, because about half of all Belgian rheumatologists were involved in this large multicentre study.

Aletaha [1] also suggests that the DAS28 score places undue emphasis on erythrocyte sedimentation rate (ESR), and thus it may misrepresent disease activity in the lower ranges [2,5,6]. We evaluated coefficients and weighting of the DAS28 score by means of a discriminant analysis. The coefficients obtained by discriminant analysis were similar to

Table 1

Coefficients of the DAS28-ESR versus the coefficients of the discriminant score obtained in the study

Parameter	DAS score	Discriminant score
Sqrt(28 TJC)	0.56	0.52
Sqrt(28 SJC)	0.28	0.28
Ln(ESR)	0.70	0.56
Patient's global VAS	0.014	0.025

DAS28, Disease Activity Score; ESR, erythrocyte sedimentation rate; Ln, natural logarithm; SJC, swollen joint count; Sqrt, square root; TJC, total joint count; VAS, visual-analogue scale.

the coefficients of the DAS28. A 20% difference was observed for the coefficient of ESR (Table 1), suggesting that ESR might be slightly over-weighted in the DAS28. In our study, this difference in weight of the ESR did not induce a significant difference between the discriminant score and the DAS28. The absolute difference between the discriminant score and the DAS28 was similar in the higher and the lower ranges of disease activity.

Finally, we agree that the different DAS variants may have strengths in specific situations. In our analysis, we found that the DAS28-ESR correlated slightly better with the decision to give a dose increase than the other 28 joint count disease activity scores, including Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI). This appears to contradict the findings of Soubrier and coworkers [7], who found that the SDAI performed better than the DAS28-ESR. An important difference between that study and ours is that our study was multicentre and that reported by Soubrier and coworkers was a monocentre study. In a monocentre study, it is intuitive that the SDAI will correlate better with the physician's decision than the DAS28 because the SDAI includes the physician's global visual-analogue scale (VAS). In contrast, in a multicentre study the physician's global VAS may be subject to interobserver and intercentre variability. These sources of variability may explain why the SDAI performed slightly worse than the DAS28 in our multicentre study; the DAS28 does not include the physician's global VAS and weights the swollen joint count lower than the SDAI.

To conclude, the analysis that we performed supports the validity of the DAS28 score for measuring disease activity in the follow up of RA patients undergoing anti-tumour necrosis factor treament. Variants of the DAS28 have been described, and each variant may have pros and cons in certain situations.

Competing interests

The authors declare that they have no competing interests.

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