Author's response to reviews

Title: Relationship between time-integrated disease activity estimated by DAS28-CRP and radiographic progression of anatomical damage in patients with early rheumatoid arthritis

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Relationship between time-integrated disease activity estimated by DAS28-CRP and radiographic progression of anatomical damage in patients with early rheumatoid arthritis

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REVIEWER N 1

Point 1. Abstract. According to the reviewer indications, we added the following sentence in the abstract “the percentage of patients with erosive……”

Point 2. Patients and methods. Laboratory investigations. We specified that the titre > 40/UL/ml of IgM-RF was considered as positive.

Point 3. Patients and methods. Statistical analysis. The sentence was completed “The reliability of the radiographic scores was assessed….“

Point 4. Results. The smallest detectable difference of a scoring method (e.g., of the Sharp/van der Heijde radiographic score) can be used as a threshold level for clinically relevant progression (Lassere M, Boers M, van der Heijde, Boonen A, Edmunds J, Saudan A, Verhoeven AC. Smallest Detectable Difference in radiological progression. J Rheumatol 1999;26:731-9). This approach was adopted in the present study of radiographic scores. The SDD defined as that amount of difference for which anything smaller cannot be reliably distinguished from random error in measurement, and therefore can be taken as “real.” The SDD can be determined using the 95% confidence interval of the standard deviation of the error of 2 (or more) measurements (limits of agreement method of Bland and Altman). An average threshold for clinically important progression might facilitate the interpretation of radiological outcomes of clinical studies, and make it possible to perform a responder analysis in clinical trials using radiological data. An opinion-based approach, that would lead clinical expert to change their therapy, seemed to be a valid and logical step, after determining the SDD, in radiological joint damage caused by rheumatoid arthritis. In this respect, is therefore, correct to assess the increase in radiographic damage also for non-progressors.

Point 5. Results. We have modified the sentence according to the reviewer indications: DAS ->DAS28 and we changed the AUC values that were erroneously reported as inverted.

Point 6. Discussion. As underlined by the reviewer, the sentence was modified to improve its intelligibility