Reviewer's report

Title: Factors predicting change from the initial DMARD treatment during the first 2 years of Rheumatoid Arthritis: Experience in the ERAN inception cohort

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Reviewer: Johannes Nossent

Reviewer's report:

General comments

The authors report data from a multicenter observational study of new onset RA patients diagnosed, treated and followed for 2 years by a rheumatologist between 2002 and 2009. They found that approximately half of all patients needed a change in DMARD and that higher HAQ, poor mental health, extra-articular disease at baseline increased the likelihood of changes, while initial use of triple DMARD reduced this likelihood. These results are mainly confirmatory as indicated by the last sentence of their conclusion. The study cohort is sizeable and reflects a real life situation, which makes the results believable. Confounding associated with all observational studies (e.g. differences in timing, type and dosage of DMARD therapy between centers) and some methodological issues are a concern.

Specific comments

- The title should reflect that the authors studied baseline predictors only.
- There is an error in the percentage in the result section of the abstract. 410 patients equal 53.5%.
- Patients were included following a first diagnosis of RA by a rheumatologist, which is a rather broad inclusion criterion. The authors have data on fulfillment of ACR87 criteria (page 8), but they do not provide or analyze such data. This would give the reader an additional idea about the cohort’s representativeness.
- The use of the DAS28-ESR is not without problems given the contribution of anti-IgG and anti-CCP antibodies to ESR. Do the authors have data on DAS28-CRP?
- Seropositive patients were RF or ACPA positive, but there is a worldwide lack of standardization for RF. Was an effort made to standardize (or control for differences in) RF measurement in the 22 different locations? If not, the use of ACPA would be more reliable as a marker of “seropositive” RA.
- The statistical analysis is unclear to me. It looks like the authors performed logistic regression (LR) on many, but not all variables shown in Table 1. They seem not to have selected the parameters that were statistically significant in univariate analysis as one would expect. In addition, while they mention that LR was used to detect independent associations with DMARD change, I cannot see that the data in Table 2 represent a true multivariate analysis given the lack of
entry data for this model.
- Based on the DMARD data given in the results section
  - SSZ monotherapy patients were less, not more likely to be seropositive (page 10)
  - The sentencing in the last paragraph on page 10 following the three main
groups is unclear and confuses the reader as to the remainder of the actual
DMARD therapies started. I would suggest a short table to clarify this.
  - The grouping of initial DMARD treatment in Table 1 is debatable. Any form of
combination should be grouped together, preferably those containing the anchor
drug MTX. While the authors refer to this in the discussion on page 13 last
paragraph, they should provide more own evidence.
  - The second sentence on page 11 (‘significant heterogeneity was found…”) is
incomprehensible. What was actually compared in the statistical analysis?

**Level of interest:** An article whose findings are important to those with closely
related research interests

**Quality of written English:** Needs some language corrections before being
published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

No competing interests