Reviewer’s report

Title: Evaluation of hand bone loss by digital X-ray radiogrammetry as a complement to clinical and radiographic assessment in early rheumatoid arthritis. Results from the SWEFOT trial.

Version: 1 Date: 23 December 2012

Reviewer: Elisabeth Lie

Reviewer’s report:

This manuscript includes some interesting data and reads fairly well. However, not all previous reviewer comments have been addressed appropriately. These are my specific comments:

Major:
- p. 8, 2nd line of last paragraph: “T-SHS” should be changed to “Change in T-SHS” – even though “radiographic progression” is included earlier in the sentence. “Change in T-SHS” should also be included within the brackets for the comparisons of RF pos. vs. neg. and men vs. women.
- p. 8-9: Please include the OR (95% CI) for radiographic progression in patients with T-SHS >5 at 12 months vs. those with T-SHS <=5 at 12 months
- The lack of statistical power – with only 23 patients being categorised in the group with HBL between baseline and 12 months – is an important issue with this paper and must be discussed (Reviewer 2, C-2). This is currently not discussed at all.
- The numbers with HBL in each of the treatment groups should be added to figure 1 t, as reported in the response to Reviewer 2, C-2, even though the percentages are reported on p. 10.
- On p. 11 negative results for some results the effect of HBL on radiographic progression within the MTX mono and MTX+INF groups are reported (two last paragraphs). These results are influenced by lack of statistical power, with only 2 and 9 patients, respectively, with HBL in these treatment groups. Please modify or discuss/comment. This also holds true for the comment in the Discussion (p.13, 1st paragraph) – “In contrast, no association was seen...” – this sentence should be removed, as the authors did not have sufficient statistical power to assess this.
- It is unclear for me why only 21+123=144 patients were included in the analyses for Figure 3 – while it is reported that 159 patients had data for DXR analyses. Were missing data in these 15 patients due to lack of 24-month radiographic data? Please report/clarify in the manuscript main text.

(Furthermore, the response to Reviewer 1 (C-7-1) is somewhat confusing as figure 2 does not include clinical data – and in table 2 data for 144 patients is reported for radiographic progression and data for 146 patients is reported for
- The data about specificity/sensitivity as HBL as a predictor of radiographic progression that is given in response to Reviewer 1 in comment C-4 should be included (with % sensitivity) in the text as this is important for the clinician and also represents a limitation.

- Reviewer 1, C-10: I believe that x-axis of the cumulative probability plot is conventionally labeled by “Percent of patients” with scaling of 0-100% along the axis. Thus, the median radiographic progression etc. in each group can be read from the figure. Please include this.

- Discussion p. 13: The information that no patients were excluded due to severe joint damage or prosthesis should rather be moved to the results.

- Reviewer 3, comment C-3 (and C-4): The rationale for performing/not performing, or including/not including, multivariate analysis seems very unclear. Firstly, with only 43 patients with 24-month radiographic progression, the statistical power is limited and only a few (around 4) independent variables could be included in the model. The authors state that they “do not believe that multivariate analysis is necessary”, but also report that these results will be reported separately. Please clarify. To be able to decide on (clinical) usefulness, the reader must have some information on how 12-month HBL compares to other predictors – such as 12-month radiographic score (see comment above), area under the curve (AUC) for ESR, CRP and DAS28 the first year etc., as DXR represents one extra measure, with extra costs associated.

Minor:

- p. 6: The third and fourth paragraphs both describe why the threshold of 2.5 mg/cm/month was selected for HBL, and they should be combined.

- Statistical analysis: The approach with doing pairwise comparisons when the ANOVA/Kruskal-Wallis p-values were statistically significant (as addressed by reviewer 1, C-6-1) should be referred to.

- Please rewrite the sentence “A similar analysis for increase...” on p. 11.

- Discussion, p. 14: [...HBL was defined as DXR-BMD change rate >= 2.5 mg/cm2/month and was used as cut-off” – please rewrite for clarity.

- Discussion p. 15: “however, this treatment may also partly conceal the positive predictive value...” – please rewrite

- Headers of tables 1 and 2: Please include “N=” before the numbers of patients in each of the groups

- Tables 1 and 2: 2 decimals are given for the means and SDs for ESR and CRP. Since the values of ESR and CRP (for each patient) are given without decimals, only 1 decimal should be included for means/SDs.

- The answer to Reviewer 2’s comment C-11 is not satisfactory as one should be aware of numerical differences in important potential confounders (such as ESR, THS, ES) in a setting with lack of statistical power (and as THS and ES are dichotomized, p-values will typically be higher for these two variables than for
continuous variables).

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests