Author's response to reviews

Title: Beyond the assessment of radiological progression in rheumatoid arthritis - The imaging of structural integrity

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Author's response to reviews: see over
Authors response to review

Title: Is there a role for Digital X-ray Radiogrammetry as surrogate marker for radiological progression and imaging of structural integrity?

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Authors response to reviewer 1:

This is an interesting manuscript studying the change in radiographic destruction by the Sharp score and by DXR (BMD, MCI, CT and W) after a mean follow-up of 22 months in RA patients treated with MTX or LEF. No change was found in the Sharp score while DXR-BMD decreased significantly by 4.3% in patients treated with MTX and by 1.4% in patients treated with LEF. However, since the patients are not randomized to be treated with MTX or LEF a comparison between the change in DXR between the treatment groups should be avoided.

Major Compulsory Revisions

1. Since I do not think that the title of the manuscript describes the contents I suggest a new title reflecting the contents.

Thanks a lot for this comment. We changed the title from “Beyond the assessment of radiological progression in rheumatoid arthritis – The imaging of structural integrity –” into “Is there a role for Digital X-ray Radiogrammetry as surrogate marker for radiological progression and imaging of structural integrity ?”.

See page I and II.

2. This is not a randomized trial. Therefore comparisons between the changes in radiographic destruction and in DXR variables between the treatment groups should be omitted. The changes within each treatment group tested with Wilcoxon signed-rank test can remain unchanged. It is written in the method section that the patients
were treated with LEF in case of contraindications to MTX. Thus, there is a clear selection bias and therefore comparisons between the groups should be avoided.

Many thanks for this important contribution. We clarified the discussion and eliminated the section with the direct comparison of the two treatment groups. Additionally, we discussed this fact as an potential limitation. Furthermore, we changed figure 1 and avoided the comparison of the two treatment groups. We changed the figure 1 in to a comparison the between Sharp Score, the DAS28 and the DXR-BMD for the total study cohort.

See page 7; page 8, paragraph 1 and also page 18, figure 1.

3. DXR-BMD has previously been found to be related to laboratory measures of inflammation, for instance ESR. How did the inflammatory activity and DAS28 change in the MTX and the LEF group and was the change in inflammation related to the alterations in the DXR variables?

Thanks a lot for this very excellent comment. We added a separate paragraph showing the changes of the disease activity parameter (ESR, CRP and DAS28) in the section results as recommended by the reviewer. The data management was performed by Sanofi Aventis. Furthermore, we changed figure 1 which compared the changes of disease activity, the Sharp Score and the DXR-BMD.

See page 5, paragraph 2 and page 18, figure 1.

Methods

4. Patients on LEF had contraindications to MTX. Please describe which contraindications.

We described the contraindication for MTX in detail.

See page 2, paragraph 2.

5. Was treatment with glucocorticosteroids (oral or injections) allowed? Please add the information in the methods.

Thanks a lot for this very important comment. The treatment with oral glucocorticosteroids was allowed for both treatment cohorts.

See page 2, paragraph 2.
6. Should the patients have a certain level of decease activity to be included? Please clarify in the methods.
There was no specific disease activity, which was determinated as an inclusion criteria. We clarified the inclusion criteria.
See page 2, paragraph 2.

Baseline data
7. The meantime from RA symptoms to diagnosis is given but information about the variability, for instance as SD, is missing. Also, the time from diagnosis to be included in this study is missing. The variability of the mean observation period is also missing as well as the variability of the MTX dose.
Many thanks for these comments. We added the Standard Deviations as recommended by the reviewer. Additionally, we provide the data of the time from diagnosis to study inclusion. We also added the variability of the MTX dosage.
See page 5, paragraph 1.

8. The mean observation period is written to be 1.8 years in this section and in other sections of the manuscript 22 months. Please change to 22 months in the whole manuscript.
Done.
See page 5, paragraph 1.

9. Please add information about the Sharp score and HAQ at baseline in table 1.
We added the informations regarding the Sharp Score at baseline in table 1. Unfortunately, the HAQ was not evaluated in the study program and in this context we can not present any HAQ-data.
See page 16, Table 1.

10. Please add information about the variability of some of the variables in table 1 where it is missing.
Done.
See page 16, Table 1.
Table 2 and figure 1

11. Please add information about the variability of the mean differences and the relative changes in table 2.
Done.
See page 17, Table 2.

12. Change the contents of the description of the figure according to point 2 above.
We changed the figure 1 in comparison of the Sharp Score (Erosion Score and Joint Space Narrowing Score), DXR-BMD and DAS28 for the complete study cohort.
See page 18, figure 1.

Minor Essential Revisions

Discussion
13. Treatment with bisphosphonates and with HRT seems to have bone protecting effects also some time after discontinuing with the treatment (in particular bisphosphonates). This can be mentioned in the discussion since it is only written in the method section that intake of bisphosphonates or HRT was not allowed during the study period.
Thanks a lot for this relevant comment. We discussed this comment extensively.
See page 8, paragraph 1.

Discretionary Revisions
14. Table 1 – Rheumatoid factor instead of Rheuma factor
Done.
See page 16, Table 1.