Reviewer’s report

Title: Novel optical spectral transmission (OST) guided versus conventionally disease activity guided treatment: study protocol of a randomised clinical trial on guidance of a treat-to-target strategy for early rheumatoid arthritis

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Reviewer: Dennis Lendrem

Reviewer's report:

This is an important trial comparing two treat-to-target strategies - DAS vs HandScan - in early RA.

Recommendations:

The authors might consider bringing the rationale for not using DAS or Boolean remission up-front in the Background or Methods. Currently it is tucked away on Page 12, Paragraph 2, Lines 293-300 of the Discussion.

The Treatment Strategy, Escalation Strategy, De-Escalation Strategy and the strategy for dealing with Adverse Events to DMARDs are all well described. However, the authors might consider including a sentence or two on how they plan to deal with potential imbalances in the two arms. Potentially, one or other treatment arm might include an excess of patients switching to LEF from MTX? Page 8, Line 194.

Currently the measures taken to prevent large deviations in HandScan and DAS-Guided treatment are somewhat sketchy - see DASPrevention of Under- and Over-Treatment in the HandScan Arm Page 9, Line 204. More detail is needed where "measures are taken" potentially leading to a switch to the "clinical arm". I thought it was unclear who would be making this decision, what data would be reviewed, when and by whom or by what?

Missing Data. The authors might consider clarifying Missing Data procedures. Especially, the decision to switch from LOCF to multiple imputation methods. Currently Page 10, Line 244 specifies multiple imputation will be used if >10% of the data are missing. However, this may or may not be appropriate depending upon the patterns of missing data. In addition, the authors state that imputations will be based upon baseline characteristics and known predictors without any a priori statement of those "baseline characteristics" or "known" predictors. A little more detail would be good.

Page 11, Line 268 restricts the analysis of change from baseline in radiographic scores to Mann-Whitney tests. This seems too restrictive? I'd recommend extending this to "ranks-based methods or generalized linear models" to permit adjustments for covariates.
Patient Safety Page 11, Lines 274-283. Early stopping based on AE and potential patient switching seems sensible but there is not detail on the stopping criterion - see Line 277. More detail would be good.

Page 13 I recommend that plans be made for anonymized data to be shared in a public repository in accordance with FAIR Guidelines.

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