Reviewer’s report

Title: Methotrexate therapy impacts on red cell distribution width and its predictive value for cardiovascular events in patients with rheumatoid arthritis

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Reviewer: Giuseppe Mandraffino

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Review file for Editor and Authors

Title: Methotrexate therapy impacts on red cell distribution width and its predictive value for cardiovascular events in patients with rheumatoid arthritis

In this paper, Julia Held and coll aimed to evaluate whether MTX treatment may impact on RDW also as predictive factor for CV invents in RA patients.

They analyzed the data from 385 outpatients, on different drug regimens, and concluded that MTX affects RDW but it makes difficult to use this parameter as prognostic index.

This referee has several issues to be addressed:

First, the paper is poorly written; the authors should significantly improve their manuscript, including spacing and punctuation. Also, according to the journal style, they should state if reference have to be showed before or after the full stop, consistently.

Second, the paper is a bit too puzzled; several paragraphs need to be re-organized, also avoiding repetitions.

Third, please check for every abbreviation; the authors well know that they have to extensively write the first time, then using the abbreviation.

Fourth, an issue about the statistic strategy; considering the vey low rate of CV events (6%), had they performed a power analysis before the data exploiting? Considering the whole studied population (385 pts), about 2/3 out of them were assuming MTX, and the same percentage of patients on treatment experimented a CV event.

moreover, it is unclear whether different drugs were prescribed to different clinical subsets of patients (this is an unavoidable bias of retrospective studies); different patient subsets may have different CV risk at baseline. Also, it is unclear how CCS use is distributed in the study population, and its impact on CV prognosis.

Fifth, it seems that baseline CV risk (including the prevalence of known CV risk factors: arterial hypertension, dyslipidemia, diabetes mellitus, smoking habit, family history, …) of enrolled patients has not been evaluated, as well as the co-administration of drugs potentially able to modify CV outcome (statins, beta-blockers, ASA, RAAS inhibitors, …).

The authors should clearly explain how they managed the potential confounders, and the actual strength of their statistic strategy (event rate seems to be too low, and too low more when you are considering the combination of event rate with so many regimens).

Last, please thoroughly check for why you lost so many in-text references: (Error! Reference source not found.).

At this point of the academic revision, I cannot go further without the authors address these main points.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

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