Reviewer’s report

Title: Relationship between Azathioprine Metabolites and Therapeutic Efficacy in Chinese Patients with Neuromyelitis Optica Spectrum Disorders

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Reviewer: Noriko Isobe

Reviewer’s report:

Li et al. aimed to find predictive biomarkers for azathioprine (AZA) efficacy in neuromyelitis optica spectrum disorders (NMOSD), associations between AZA metabolites concentration and clinical outcomes which represent immunosuppressive efficacy was investigated, which was followed by association study between AZA metabolites concentration in erythrocytes and polymorphisms in nucleoside transporter genes. They found the link between greater improvement levels in annual relapse rate (ARR) and higher concentration of AZA metabolites, especially 6-TGNs. Additionally, some pharmacogenomic results showing links between 6-TGNs levels and SNP genotypes in SLC28A3, coding nucleoside transporters, were also provided.

Although the study was well designed, there are some issues to be addressed.

Main comments;

1) ARR improvement was defined as the difference between pre-therapy ARR and post-therapy ARR divided by the pre-therapy ARR. Suppose ARR decreases (disease improves after treatment), is the value negative or positive? If it is negative, the R values in Table 3 will be negative. Please clarify the formula to calculate ARR improvement or at least specify in which way the ARRs are subtracted. Furthermore, it will be helpful for readers to see plots between ARR improvement vs. 6-TGNs and 6-MMPNs.

2) Although the term of relapse is defined in the Method section, it is not clear how samples were categorized whether they were taken during relapse or remission phase. Please define more clearly what non-relapsed or relapsed mean.

3) Please provide information why those SNPs were selected for genotyping out of all the variants in SLC28 or SLC29. Additionally, in the supplementary data, other variants in ABCB1, ABCC4, etc. were also included.

Minor comments;

1) The names of the tables and supplementary tables in the text do not match with the actual tables.
2) Discussion, 4th paragraph; Typos for TMPT (x TPMT).

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.

Yes

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

Yes

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 am able to assess the statistics

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

Acceptable

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