Author’s response to reviews

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

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Author’s response to reviews:

Dear Dr. Tjalf Ziemssen,

We are pleased to resubmit the revision of our manuscript "Relationship between Azathioprine metabolites and Therapeutic Efficacy in Chinese Patients with Neuromyelitis Optica Spectrum Disorders" (NURL-D-17-00010). We appreciated the valuable and detailed comments from the reviewers. In addition to the point-by-point responses, we have provided our responses to the items from the editors below. All changes to the manuscript are indicated in the text by highlighting. Please do not hesitate to contact us if you have additional suggestions on improving the paper. We will not be able to add, remove, or change the order of authors once the editor has accepted your manuscript for publication.

The point-by-point responses

Byung-Jo Kim (Reviewer 2):
1. Q: The authors stated this study was prospectively designed. They enrolled subjects using the International Consensus Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorder 2015. If this study prospectively enrolled subjects with the criteria, this study could not have subjects with follow up duration for 40 months. Of course, the criteria were released at many international congresses related to MS and NMOSD from 2014, but it was still impossible to have subjects with follow up period more than about 2 years. So please make sure this is a prospective study or study analyzing clinical characteristics of subjects who was prospectively enrolled for AZA metabolites and genetic polymorphism.

A: What you questioned is quite important. It is a study analyzing clinical characteristics of subjects who was prospectively enrolled for AZA metabolites and genetic polymorphism. We had started collecting NMO patients based on the criteria (Neurology. 2006, 66(10):1485-1489) and NMOSD patients based on the criteria (The Lancet Neurology 2007, 6(9):805-815) since 2 years ago. After the International Consensus Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorder 2015 was published, we re-diagnosed all the patients enrolled and selected patients who met the diagnosis of NMOSD (Neurology 2015; 85:177-189). We have clarified it in the manuscript (please see Methods-subject section, line 3, page 3).

2. Q: Reference # 2 is not about the criteria 2015.

A: We have corrected the Reference number. (please see Methods-subject section, line 18, page 4).

3. Q: A sentence for limitations was written. Please describe more about reason why the study for efficacy of AZA in especially patients with NMOSD needs longer follow up period.

A: We appreciate reviewer’s comments. We have added the reason in the last part of discussion, as follow:” However, the disease activity of NMOSD is highly variable by individual subjects and some patients show the AZA efficacy showed after 6 months to 18 months”. (please see discussion section, line 53, page 7).

Best wishes to you.

Xinghu Zhang