**Reviewer’s report**

**Title:** Peripheral blood lymphocytes immunophenotyping predicts disease activity in clinically isolated syndrome patients

**Version:** 0  **Date:** 03 Jul 2016

**Reviewer:** Jen Jen Su

**Reviewer's report:**

Page 2:

1. Introduction:

Paragraph 1, Line 4: Mc Donald's --> additional space

Paragraph 2, Line 1: cerebrospinal-fluid --> abbreviation needed and hyphen unnecessary

Line 3: OCBs --> no whole name at previous lines

Page 3:

1. Introduction:

Last paragraph: the control group is not apparent for the study

2. Material and Methods:

2.1 Study population

Paragraph 1, Line 3: presence of > or = 2 T2-hyperintense lesions --> CIS can be recognized as one attack with suspected demyelinating lesion in brain, just one is also considered, if the study needed two or more T2 lesions, is it fulfilled with definition of CIS or it had already been diagnosed as Multiple sclerosis with lesions of DIS?

Line 2-3: about the EDSS --> it is estimated as initial attack? or after treatment of steroid therapy to remission stage?

Paragraph 2: the number of Medical Ethics Committee lack

Page 4:
2.2 Study outcomes:

Paragraph 1, Line 6: the definition of CDP based on an increase in EDSS by 1.0 point, if baseline EDSS > 0, or by 1.5, if baseline EDSS = 0; basically the progression type MS should be relapsed before for several times then enter the stage of progression, if the patient had EDSS just 0 before and diagnosed as CIS, is it enough to define as progression type just during 6 months; besides, if the patient had severe attacks before, then EDSS increased significantly, but it should be considered as relapse but not progression.

Page 9:

4. Discussion

Paragraph 1, Line 2-3 --> I cannot recognize what the meaning the author want to express from the two lines

paragraph 2, Line 3-4 --> how to explain teh value of CD4+ T lymphocyte in your CIS patients at baseline were lower than MS?

Page 10:

Paragraph 2, Line 4: Up regulation of naive CD45RA+T -lymphocyte and parallel down regulation of memory CD45+RO+ cells ... --> what is the meaning for the Linomide to correlate with your study?

Paragraph 3, Line 6: is the slight reduction of total CD45RA+ lymphocyte shown any statistically significant to clinical worsening?

Page 11:

Paragraph 1, Line 9-11: the lower levels of B cells means less production under stimulation of interferon or other factor? Traditionally, B cells is less considered as the major role to convert CIS to CDMS, how to explain the so-called lower levels of B cell, but more prominent conversion rate to MS?

Page 12: natural killer cell should be abbreviated as NK cell

**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.

No

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

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Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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