Author's response to reviews

Title: Free radical scavenger, edaravone, reduces the lesion size in human brain ischemic stroke

Authors:

Taizen Nakase (nakase@akita-noken.jp)
Shotaroh Yoshioka (shotaroh@akita-noken.jp)
Akifumi Suzuki (akifumi@akita-noken.jp)

Version: 4 Date: 3 September 2010

Author's response to reviews: see over
Dear Dr. Alam:

MS # 2125320439393187
Title: Free radical scavenger, edaravone, reduces the lesion size in human brain ischemic stroke

Thank you for your effective suggestions. We have responded to the reviewers’ comments as accurately as possible. Moreover, we newly added the data regarding NIHSS on admission and at discharge. We found that the significant neurological improvement was observed in edaravone treated small-vessel occlusion group. We also asked to a statistician again and completely renewed Figures 2 and 3, as reviewers have concerned. Please find enclosed our revised manuscript, “Free radical scavenger, edaravone, reduces the lesion size in human brain ischemic stroke”.

We hope that the paper will gain the satisfaction of the journal.

Revised points were precisely described below:

To Reviewer1(Dr. Lapchak)’s comments,

We have mentioned the review of Dr. Lapchak in the manuscript (p8 line11-13). Then, we have changed the sentence in the conclusion following the suggestion (p10 line7-10).
Following minor issue1): We have changed all graphs making them easy for understand and described labels of the graphs precisely. Figure legends were also corrected.

Following minor issue2): We asked a native English speaker for correcting the text and described in the acknowledgement section (p10 line11-13). He is a sophisticated researcher with plenty of scientific knowledge.

Following minor issue3): We corrected all misspelling throughout the manuscript.

Following minor issue4): We erased the sentence from abstract (p2 line23) for avoiding misreading, as suggested.

Following minor issue5): We described precisely about the selection of acute stroke patients in the methods section (p4 line22- p5 line8), and explained the reason why our study was not a parallel design but a 2-year sequential design (p9 line25- p10 line1).

Following minor issue6): We corrected the tense in the methods section as suggested.

Following minor issue7): We changed the word ‘prognosis' to the activity of daily living (ADL) level, for avoiding misunderstand (p6 line2-7). In our hospital, all patients were assessed by neurologists or neurosurgeons using NIHSS. In this study, we used these data recorded on patient’s clinical record. We checked mRS at one year following the onset by using outpatient’s record.

Following major issue1): The medical treatments in this study were approved by the committee of medical ethics. We described this fact in the text (p4 line23- p5 line2). Edaravone is actually Radicut®. We also wrote about the medication precisely in the methods section (p5 line5-8).

Following major issue2): We corrected the number in the abstract (p2 line9-10). It was a simple mistype.

Following major issue3): We agree the reviewer’s comment. We also checked ongoing clinical trials on the website and mentioned in the discussion section (p10 line2-6). Then, we removed the sentences which were pointed out by the reviewer from the discussion section.

Following major issue4): We explained the discrepancy of the clinical outcome between our observation and previous reports in the discussion section (p9 line6-17).
Following major issue 5): We rewrote the conclusion, as the reviewer suggested (p10 line 7-10).

Following major issue 6): We rewrote the whole discussion section, as the reviewer suggested (p8 line 3- p9 line10).

Following major issue 7): We rewrote our conflicts of interest (p10 line 15-18).

To Reviewer2(Dr. Emsley)’s comments,

We referred STAIR reports and mentioned more recent studies to make the background of our study clearer, as the reviewer suggested (p4 line1-19).

Of course, all patients in our hospital were diagnosed by neurologists and neurosurgeons clinically. MRI is also used for the assistance of the diagnosis. For avoiding the misread, we rewrote the sentences in the methods section (p5 line8-10).

Following the reviewer’s comment, we added the NIHSS data in the manuscript (p6 line2-5). We also asked about the statistical analysis to a statistician, who is well known person in the field of Japanese Stroke Statistics. Then, the figures were changed, and we rewrote the text in the statistical analysis paragraph (p6 line8-16).

Following the reviewer’s comment, we precisely described patients’ background in the Table1.

We agreed the reviewer’s comment, and changed the Figures 1 and 2. Moreover, we described more precisely about the calculation of the lesion size alteration (p5 line23-26). We understood and agreed the reviewer’s comment. We changed the title (p1 line2-3), and we rewrote the sentences about the findings of small-vessel occlusion patients (p8 line24-p9 line17).

Following the reviewer’s comment for the discussion section, we rewrote the discussion sentences and referred papers which mentioned the effect of edaravone on the injured endothelia (p8 line5-8).

Following the reviewer’s comment, we changed the whole sentences regarding the limitation of our study and the importance of clinical research of the effect of edaravone on
the ischemic stroke patients (p9 line25- p10 line6).

To Reviewer3(Dr. Unno)’s comments,

Following the reviewer’s comment#1: We mentioned about the methods of lesion measurement with references (p5 line18-21).

We agreed the reviewer’s comment#2, and all stroke subtypes were renamed following TOAST category.

Following the reviewer’s comment#3: We added the average infarction volume in each stroke subtype in Table 2.

Following the reviewer’s comment#4: We described the result of lesion size which was observed sooner reduction in edaravone treated group compared to edaravone non-treated group (p7 line2-8). Then, we discussed about the difference of reduction rate of ischemic lesion between edaravone(+) and (-) groups (p8 line14-23).

Following the reviewer’s comment#5: We described the number of patients in Figure 2.

We agreed the reviewer’s comment#6, then we rewrote the sentences in which neurological disability at one year after the stroke was mentioned (p7 line23- p8 line2).

Following the reviewer’s comment#7: We changed the title (p1 line2-3) and conclusion (p10 line7-10). We also defined the sentences mentioning the reduction of ischemic lesion was observed faster in edaravone treated group compared to non-edaravone treated group (p8 line14-23).

Following the reviewer’s comment#8: We rewrote the limitation of our study in discussion section (p9 line25- p10 line6).

Throughout the text, we corrected grammatical errors and changed sentences to avoid misreading. We also arranged the text for keeping the consistency of the outline.

Thank you for your consideration.
Sincerely yours,

Taizen Nakase

Encs.