Author's response to reviews

Title: Study protocol: Safety correction of antipsychotic polypharmacy with high dose in Japan

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Author's response to reviews: see over
Covering letter

Dear Editor of Bio Med Central Psychiatry:

We are enclosing a manuscript entitled, “Study protocol: Safety correction of antipsychotic polypharmacy with high dose in Japan” for consideration for publication in Bio Med Central Psychiatry. This work has not been previously published, is not being considered for publication elsewhere, and has been read and approved by all authors. This work has also been approved by the Ethics Committee of Tottori Medical Center. Informed consent of the subjects was obtained and their anonymity was preserved. This study was performed with a Research Grant from the Ministry of Health, Labour and Welfare, Japan. Conflicts of interest were as follows. Dr Sukegawa has received grants from Otsuka. Dr Inagaki and Dr Yoshio have received grants from the Japan Pharmaceutical Manufacturer Association. Dr Inada has received lecturer’s fee from Otsuka, Dainippon Sumitomo, GlaxoSmithKline, Eli Lilly, Janssen, Astellas and Mitsubishi Tanabe. Dr Iwata has received lecturer’s fee from Otsuka, Janssen, GlaxoSmithKline, Shionogi and Eli Lilly, grants from Otsuka and bounties from Otsuka, Dainippon Sumitomo, GlaxoSmithKline, Mitsubishi Tanabe, Yoshitomiyakuhin and Eizai. Other authors have no potential conflicts of interest that were disclosed.

The number of tables is 3 and the number of figures is 0. We appreciate your review of this work.

The Manuscript was changed some points by suggestions of editorial office

1. The names of participated facilities were added to acknowledgements.

2. Period of data collection was added page 11, line 17 as “The subjects were recruited by the psychiatrists participated this research, from Nov 1, 2010 to Mar 31, 2012, and
the data was fixed at Jan 31, 2013. 163 patients were enrolled and assigned to the dose reduction group and the control group, 101 and 62 respectively.”

3. SCAP study is different from RAS study. It was added in page 12, line 2 that “The amounts of antipsychotics were reduced in the RAS study and the SCAP study with the same method, but two studies were different. The RAS study was completed by Dec 1, 2007. The SCAP study was started at Nov 1, 2010.”

4. How to assign to the groups was added in page 10, line 10 as “Each subject was assigned to dose reduction or control group, with complete randomization of 1:1 probability decided at Fujita Health University.

How to recruit was written in page 11, line 17 as “The subjects were recruited by the psychiatrists participated this research”.

Sample size calculation had been written in page 10, line 8 as “Sample size was estimated for the clinical study to allow explanation of non-inferiority of dose reduction group compared to control group in primary evaluation scale based on binary set-up repeated measurement linear mixed model. According to the customary practice, in “ANOVA: repeated measures, between factors”, if $\alpha$ error was 0.025 (in order to analyze multiple scales), statistical power was 0.8, non-inferiority margin of Cohen’s $d$=0.2 (it was predicted that the difference was smaller than moderate), correlation among rep measures=0.5, and number of measurement was 6 times then the calculated n was $n=142$. Based on this, the target number of cases was 72 for each group.”

5. The difference of SCAP study and The RAS study was added in p12, line 7 as “For convenience to participated psychiatrists, we made the reduction speed table of
antipsychotics in the SCAP study. This had not yet been made at the RAS study. In the RAS study, participated psychiatrists calculated their reduction amount by themselves.” and in line 17 as “These points were different from the RAS study. In the RAS study, only inpatients were acceptable, treatment with more than 3 antipsychotics at more than 1500 mg CP, and follow-up period of 9 months in both the dose reduction and the control group.

6. Others

Page 11, line 5, “J Tottori Clinical Science” was corrected to “Tottori J Clin Res”

Page 21 and 22, in legends of table 2 and 3, (Cited and partially modified from Sukegawa11) were corrected to (Cited and partially modified from Sukegawa [11])

After submission, I noticed that “J Tottori Clinical Science” in page18, line2 was not deleted. I submit again delete the “J Tottori Clinical Science”.

Sincerely yours,